·英文来稿·

Computed tomography versus transthoracic echocardiography in the detection of complex congenial heart diseases in china: a meta-analysis

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【**Abstract**】 **Objective**: To perform a meta-analysis to evaluate the diagnostic performance of computed tomography (CT) and transthoracic echocardiography (TTE) in complex congenital heart diseases (CHD) in China. **Methods**: MEDLINE, Cochrane library and China National Knowledge Infrastructure (CNKI) database from January 1966 to October 2010, were searched for initial studies in China. All the studies, published in English or Chinese, used TTE, CT, or both as diagnostic tests for CHD and reported the rate of true-positive, true-negative, false-positive and false-negative diagnoses of CHD from TTE and CT findings with the surgical results as the "gold-standard" (15 studies, XX patients) were collected. The statistic software package, "Meta-Disc 1.4", was used to conduct data analysis. A covariate analysis was used to evaluate the influence of patient or study-related factors on sensitivity. **Results**: Pooled sensitivity for diagnosis of CHD were 95% [95% confidence interval (CI): 94%~96%] for CT studies and 87% (95% CI: 85%~88%) for TTE studies. The difference between the pooled sensitivity of CT and that of TTE was statistically significant ($P<0.001$). TTE had higher sensitivity [0.96 (95% CI: 0.94~0.97)] for cardiac malformation but lower sensitivity [0.78 (95% CI: 0.76~0.81)] for extracardiac malformation than CT. **Conclusion**: CT can provide added diagnostic information compared with TTE in patients with CHD in China, especially for patients suspected of extracardiac malformation.

【**Key words**】 Echocardiography; Tomography, X-ray computed; Heart Defects, Congenital; Meta-analysis

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Since the last century, the management of CHD has been vastly improved, contributing to increased survival into adulthood[1-2]. This progress largely depends on the advancements of surgical repair, which would not have been possible without a clear delineation of the anatomy and physiology of the defects[3]. With the characteristics of noninvasiveness, speed, safety and easy availability, transthoracic echocardiography (TTE) is always the firstline study of choice for patients with CHD. One of its limitations is the relatively small acoustic window for which TTE may be inadequate if cardiac, thoracic and visceral anomalies are needed to be clearly delineated[4]. In recent years, CT technology has advanced rapidly, Cardiac CT which contributes to valuable information on congenital abnormalities is capable of complimenting echocardiography and replacing further diagnostic cardiac catheterization for anatomical delineation if performed with good contrast medium injection technique[5].

Although extensive research has been performed in regard to the diagnostic performance of CT and TTE for the detection of congenial heart diseases, the optimal imaging staging strategy has not yet been defined. The aim of our study was to perform a Meta-analysis to compare current CT and TTE in detecting abnormalities of heart diseases in China, which as far as we know, had not previously been studied.

Methods

1. Literature search

A comprehensive computer literature search[6] of abstracts about studies in human subjects was performed to identify articles about the diagnostic performance of CT and TTE for the detection of CHD in China. The MEDLINE databases, from January 1966 to October 2010, were searched with the following keywords: computed tomography (CT) or transthoracic echocardiography (TTE) and congenial heart diseases (or CHD) and sensitivity (or specificity, false-negative, false-positive, diagnosis, detection or accuracy). The China bio-medicine databases was used for Chinese articles with the following keywords: (CT or TTE) and (congenial heart diseases

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or CHD). Other database such as Cochrane Library, and China National Knowledge Infrastructure(CNKI) database were also searched for relevant articles. The list of articles was supplemented with extensive cross-checking of the reference lists of all retrieved articles.

2. Study selection

Three observers independently checked all retrieved articles for inclusion criteria. One observer (Z. H. C) checked all articles, and two observers checked a subset of articles: one observer (Z. L) checked studies that predominantly focused on evaluation of CT, another one (Y. J. G) checked studies that predominantly focused on evaluation of TTE. Disagreements were resolved in consensus. The inclusion criteria were as follows: ①articles were reported in the English or Chinese; ②CT or TTE(alone or in combination, but not in sequence) was used to detect CHD; ③only surgical findings were used as the reference standard; ④ for per-lesion statistics, sufficient data were presented to calculate the accuracy for imaging techniques; ⑤when data or subsets of data were presented in more than one article, the article with the most details or the most recent article was chosen; ⑥ no less than 20 patients in the study was in cluded; ⑦ studies using sequential test combinations (e. g, CT in patients selected on the basis of CDH which are not unambiguous on TTE) were excluded, because the selection of patients on the basis of diagnostic test results could have unpredictably modified the estimate of the select characteristics of the tests themselves.

3. Data extraction

The same observers independently extracted relevant data about study characteristics and examination results by using a standardized form. Observers were not blinded with regard to such unnecessary information as the journal name, authors' name and affiliation, or year of publication, since this has been shown to be unnecessary[7]. To resolve disagreement between reviewers, a third reviewer assessed all discrepant items, and the majority opinion was used for analysis.

Relevant studies were further examined with Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria[8]. To perform accuracy analyses, we extracted the following items: description of study population (age), study design (prospective, retrospective or unknown), patient selection (consecutive or not), interpretation of the test results (blinded or not). The following features were also included: as to CT, the slices of scanner were included, and as to TTE imaging, two-dimensional or three-dimensional were included. The numbers of true positive (TP), false-negative (FN), false-positive (FP) and true-negative (TN) results in the detection of CHD were extracted on per-lesion.

4. Statistic analysis

The statistical software named "Meta-Disc", version 1.40, was used to analyze data for CT and TTE. We only calculated pooled sensitivity for each modality. The Galbraith plots (visual inspection of forest plots of accuracy estimates) and a chi-squared statistical test were used to assess heterogeneity among the studies included in the meta-analysis. A fixed-effects model (FEM) was utilized if homogeneity existed among different studies, while a random-effects model (REM) was used if heterogeneity existed.

Results

1. Literature search and selection of studies

The detailed procedure of study selection in the meta-analysis was showed in Fig 1. Total of 936 initial studies were searched from all the databases. After reading the title or abstracts, we reviewed 128 studies in detail. Of all these articles, 113 were excluded because ①the aim of the articles was not to reveal the diagnostic value of CT and TTE for detection

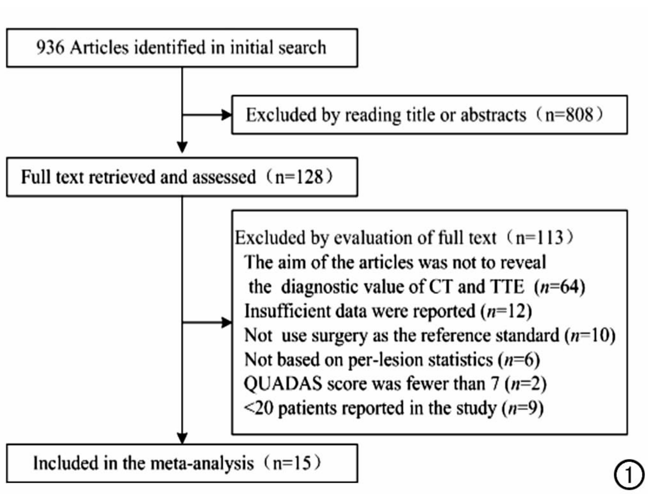


Fig 1 Article selection process.

of CHD (n=64);②insufficient data were reported to construct (n=12);③researchers in the articles did not only use surgery finding as the reference standard (n=10);④the studies were not based on per-lesion statistics (n=6);⑤the number of "yes" response to the 14 questions of QUADAS was fewer than 7 (n=2);⑥fewer than 20 patients reported in the study (n=9). Finally,15 articles[9-23] fulfilled all the inclusion criteria and were selected for data extraction and data analysis.

2. Study design characteristics

The principal characteristics of the 15 studies included in the meta-analysis is in Table 1. 635 patients were included in this meta-analysis. In the selected 15 studies,all studies were for both of CT and TTE.

3. Study quality

We used the "QUADAS" quality assessment tool to evaluate each selected study. All the eligible studies' score was more than 6 in the 11 questions (Table 2). All studies did not describe the interval time between index tests diagnostics and confirmation. Patients in most studies did not receive the same reference standard. In most of the studies, the interpretation of the reference standard results with or without knowledge of the index test results was not clear. To the other questions, the "yes" responses were more than 80.0%.

4. Summary estimates of sensitivity and heterogeneity assessing

The pooled sensitivity for CT and TTE was 0.95 (95% CI:0.94~0.96) and 0.87 (95% CI:0.85~0.88), respectively. CT had significantly higher sensitivity estimates than TTE ($P<0.001$). However, to the studies both for CT and TTE, the sensitivity were highly heterogeneous, which affected the diagnostic value. There was no heterogeneity among studies about TTE for cardiac malformation (sensitivity: heterogeneitychi-squaredwas18.34, $P=0.1917$, $I^2=$

Table 1 Participants' characteristics and types of studies included

study	No. of Patients	Rate of Men (%)	Age (Range) Mean	Blind	Study type	No. of malformation	cardiac malformation			heart-large vascular connecting and extracardiac malformation		
							CT	TTE	Surgery	CT	TTE	Surgery
Huang MP,et al[9]	48	36	2y,1m~12y	Unclear	retrospective	174	53	55	57	114	90	117
Wang RP,et al[10]	35	16	12.6y,6m~28y	Unclear	retrospective	136	43	45	47	86	53	89
Yang YY,et al[11]	25	13	—,4m~22y	Unclear	retrospective	79	27	25	29	49	33	50
Luo DD,et al[12]	112	87	11.7d,2~28d	Unclear	retrospective	368	156	157	160	202	186	208
Zhong JS,et al[13]	24	14	(8.67±6.34)y,1~18y	Unclear	Unclear	88	32	35	38	48	39	50
Guo JG,et al[14]	52	36	(14.7±6.5)y,1~37y	Unclear	retrospective	142	48	50	52	86	66	90
Huang XM,et al[15]	20	9	(11.7±12.1)y,—	Unclear	retrospective	84	22	27	29	47	42	55
Ruan WY,et al[16]	55	38	5.8m,1d~12m	Unclear	retrospective	199	62	66	68	130	67	131
Qin WH,et al[17]	35	25	2.1y,4m~15y	Unclear	retrospective	82	36	38	39	41	35	43
Wang J,et al[18]	35	20	6.5y,8m~15y	Unclear	retrospective	119	48	54	56	60	50	63
Li GW,et al[19]	39	19	16y,44d~36y	Unclear	retrospective	102	40	46	48	53	38	54
Lv JL,et al[20]	32	—	—	Unclear	retrospective	128	40	57	57	70	58	71
Wang HZ,et al[21]	54	32	10.8y,11m~45y	Unclear	retrospective	176	62	63	64	111	96	112
Xiao Y,et al[22]	23	21	(16±9)y,5~61y	Unclear	retrospective	59	18	18	19	37	36	40
Li JL,et al[23]	69	51	(18.9±36.5)m 2d~12.5y	Unclear	retrospective	129	—	—	—	—	—	—

Table 2 Evaluation of quality of included studies using the QUADAS tool

Study	Appropriate patient spectrum	Selection criteria described	<1month between tests	All received reference standard	Same reference standard	Reference standard independent	Test results blind to reference standard	Reference standard blind to test results	Clinical data available	Uninterpretable results reported	Withdrawals explained
Huang MP et al[9]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear	Yes
Wang RP et al[10]	Yes	No	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Yang YY et al[11]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Luo DD et al[12]	Yes	Yes	No	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Zhong JS et al[13]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Unclear
Guo JG et al[14]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Huang XM et al[15]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Ruan WY et al[16]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Qin WH et al[17]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Wang J et al[18]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Li GW et al[19]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Lv JL et al[20]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Wang HZ et al[21]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Xiao Y et al[22]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes
Li JL et al[23]	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes

23.7%). The forest plots for the sensitivity of CT and TTE were showed in Fig 2～7.

5. Subgroup analysis

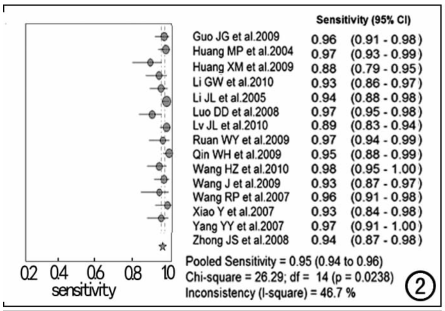
The results of subgroup analysis performed for deformity position (cardiac and extracardiac) were also presented. Cardiac malformation included atrial septal defect, ventricular septal defect, valve deformity, patent foramen ovale and endocardial cushion defects. Extracardiac malformation included patent ductus arteriosus, variation of coronary anatomy, coarctation of aorta, anomalous pulmonary venous drainage and anomalous origin of pulmonary artery.

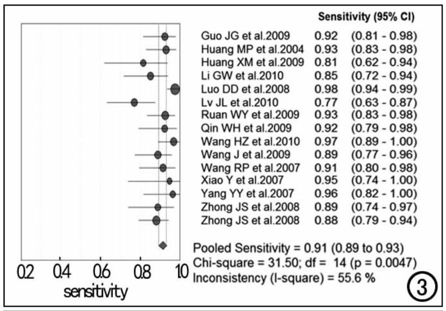
For cardiac malformation, the sensitivity of CT was significantly lower than TTE ($P<0.05$), but the sensitivity for extracardiac malformation, CT was higher than TTE ($P<0.05$). We also did a subgroup analysis for the dual-source CT, and found the sensitivity about dual-source CT was similar to the overall pooled sensitivity mentioned before.

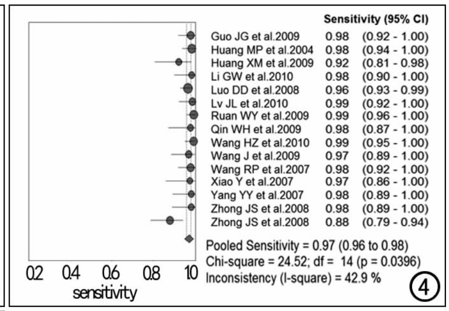
Discussion

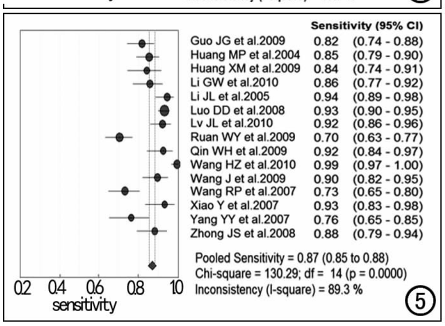
For the diagnosis of CHD, various imaging tools have been used, including cardiac catheterization, CT, echocardiography and MRI. For the past 20 years, TTE remains a first-line imaging examination in patients with suspected CHD. It is inexpensive and reproducible and demonstrates cardiac function in real time[24]. This examination method has been considered the clinical gold standard, and often can eliminate the need for cardiac catheterization. With the increased use of CT angiography, cardiac CT has shown its value of providing valuable information in the detecton of congenital abnormalities. The purpose of this study is to perform a meta-analysis to compare the diagnostic performance of CT and TTE in the diagnosis of CHD.

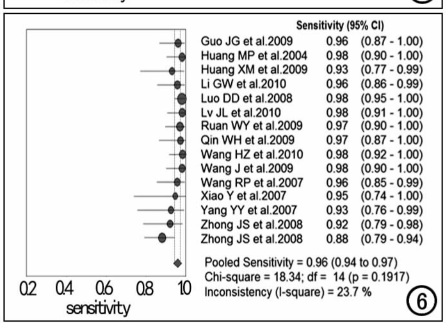
To avoid selection bias, both the MEDLINE database and the EMBASE and the Cochrane Database of Systematic Review were searched for relevant articles. In addition, all reference lists were checked manually. To minimize bias in the selection of studies and in data extraction, reviewers independently selected articles on the basis of inclusion criteria, and scores were assigned to study design characteristics and examination results by using a standardized form that was based on the QUADAS tool. The QUADAS tool is an evidence-based quality assessment tool, which was developed for systematic reviews of studies of diagnostic accuracy[25]. Data were analyzed by means of a random effects approach, which accounts











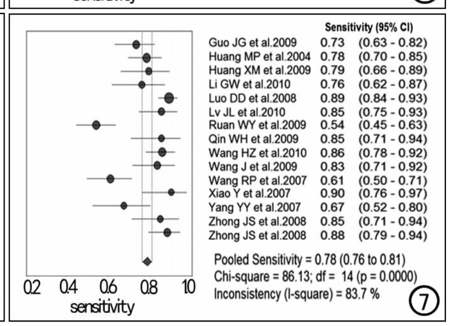


Fig 2 Sensitivities and 95% confidence intervals (CI) for studies assessing the diagnostic accuracy of CT in all malformation of CDH. **Fig 3** Sensitivities and 95% CI for studies assessing the diagnostic accuracy of CT in cardiac malformation. of CDH. **Fig 4** Sensitivities and 95% CI for studies assessing the diagnostic accuracy of CT in extracardiac malformation. of CDH. **Fig 5** Sensitivities and 95% CI for studies assessing the diagnostic accuracy of TTE in all malformation. of CDH. **Fig 6** Sensitivities and 95% CI for studies assessing the diagnostic accuracy of TTE in cardiac malformation. of CDH. **Fig 7** Sensitivities and 95% CI for studies assessing the diagnostic accuracy of TTE in extracardiac malformation of CDH.

for the heterogeneity between studies.

To our knowledge, this meta-analysis was the first report that assessed and compared summary estimates of overall diagnostic ability for CT and TTE. The results of our meta-analysis demonstrated CT had higher pool sensitivity than TTE in the detection of CHD. TTE was always a routine examination of CHD, however, TTE provided not enough information concerning heart-large vascular connecting and extracardiac malformation, which may influence the further treatment strategy. Therefore, to a highly suspected patient with heart-large vascular connecting or extracardiac malformation, additional imaging information was necessary. Regarding that CT can provide more anatomic information than TTE, CT might be helpful in the selection of patients who may derive a significant survival benefit. CT may be a more useful supplement to current surveillance techniques, particularly for those patients with heart-large vascular connecting or extracardiac malformation.

TTE has been long known to have a better performance in young children due to increased permeability of the ribs with a broader acoustic window. In our analysis, Echocardiography appears more suitable for the evaluation of lesions of the cardiac valves as well as the cardiac septa. We attribute these findings to the technical implications of each imaging modality. CT can't display function and ventricular blood flow but TTE can, which has been recognized as very useful for the evaluation of atrioventricular valve defects[26]. Moreover, the color flow Doppler feature of TTE is particularly useful for evaluating flow across atrial and ventricular septal defects, such as malformations, sclerosis and fusion[27].

However, despite its advantages in showing muscular wall movement and ventricular blood flow, TTE does have limitations compared to CT, mainly because of its limited acoustic window, Therefore, CT might be more useful for congenital coronary artery anomalies. For example, the assessment of the coronary vessels largely benefits from simultaneous delineation of the entire coronary vascular system, including its origins. Therefore, CT might be more useful for congenital anomalies of the coronary vessels.

Further analysis revealed that pulmonary stenosis and aortic coarctation are the most common diseases leading to the false positive results. Our data also indicate that CT is useful for the diagnosis of congenital anomalies of the great arteries. Finally, intra- and inter-observer variability, depending sonographer experience and relatively poor temporal and spatial resolution compared with radiologic tools are disadvantages of echocardiography. The development of new echocardiography-based technologies, including three-dimensional echocardiography and transesophageal echocardiography appears to hold significant promise to improve CHD assessment[29].

During the years, substantial improvements in CT (eg, introduction of spiral CT, multisection CT, dual-source CT) have been introduced. To account for these improvements, data for techniques were analyzed separately, and subgroup analyses were performed. The study shows that, there was no significant difference between dual-source CT and single-source CT both in cardiac and extracardiac malformation. But dual-source CT can shorten the time and reduce the radiation dose and reduce the influence of heart rate. With 256-, 320- or 640-section CT applied gradually, we believe CT can provide accurate information in the diagnosis of CHD in future.

Conclusion

This meta-analysis was the first report that assessed and compared summary estimates of overall diagnostic ability of CT and TTE that were currently used for detecting CHD in China. The results of our meta-analysis demonstrated that CT might be a useful technique for CHD, particularly for those patients with heart-large vascular connecting and extracardiac malformation, however, TTE may have additional value in detecting cardiac malformation.

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