Diagnostic Efficiency of Four-Dimensional Echocardiography plus Two-Dimensional Speckle Tracking Echocardiography in Fetal Congenital Heart Disease

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The prenatal diagnosis yield of congenital heart disease by prenatal echocardiography is only about 40 % due to the impact of multiple factors on the prenatal observation of the fetal heart. Improvement of the prenatal diagnostic efficiency of congenital heart disease is essential to reduce neonatal mortality and improve perinatal survival, which is in line with the national policy in China to improve the quality of the birth population and reduce age-related mortality. The current research was performed to evaluate the diagnostic efficiency of four-dimensional echocardiography plus two-dimensional speckle tracking echocardiography in fetal congenital heart disease. Pregnant women with fetal congenital heart malformations who underwent maternity examinations in our hospital between January 2019 and December 2021 were recruited for eligibility assessment and 140 cases were eventually included. The eligible patients were assigned to receive either two-dimensional speckle tracking echocardiography (two-dimensional group) or two-dimensional speckle tracking echocardiography plus four-dimensional echocardiography (combined group) *via* random number table method in a 1:1 ratio, with 70 cases in each group. The outcome measures for the evaluation of the diagnostic efficiency of the two means included detection rate, screening time required for different diagnostic techniques and diagnostic results. Four-dimensional echocardiography was associated with a significantly shorter disease screening time *vs.* two-dimensional speckle tracking echocardiography ($p<0.05$). Combined detection produced markedly higher diagnostic accuracy, specificity and sensitivity *vs.* single detection ($p<0.05$). Hybrid detection of four-dimensional echocardiography with two-dimensional speckle tracking echocardiography provides enhanced diagnostic efficiency and a higher detection rate for congenital heart disease *vs.* single detection.

Key words: Four-dimensional echocardiography, two-dimensional speckle tracking echocardiography, congenital heart disease, ultrasound

Recent studies have shown that congenital heart disease ranks first among all congenital malformations in newborns and its incidence is increasing year by year. Statistics show intrauterine and neonatal mortality rates as high as 85 %, especially for extra cardiac malformations with intrauterine force failure[1,2]. Previous studies suggest that the pathological mechanism is associated with environmental and genetic factors. Approximately half of the children with congenital heart disease die of severe heart disease within the 1st y of life and survivors also suffer from recurrent respiratory infections and developmental disorders during their growth and development, resulting in an unavoidable financial burden and psychological impact on the families of the affected children[3,4]. Moreover, the delivery of such fetuses increases the investment of medical resources and socioeconomic burden and decreases the overall quality of the birth population. Thus, early screening and measurement for fetal malformations are of great significance[5,6]. Currently, clinical screening methods for diagnosing fetal congenital heart disease include blood tests, electrocardiograms and ultrasound, which, however, produce poor

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detection rates are limited clinical promotion. Fetal echocardiography is one of the most accurate methods for prenatal fetal health monitoring to detect fetal heart malformations, despite its prenatal diagnosis yield of only about 40 % in congenital heart disease. The accuracy of ultrasound diagnosis of fetal cardiac malformations has been improved in recent years with the advancement of medical ultrasonography and the improvement of ultrasound instrument resolution. Echocardiography was first reported in 1972 and has been widely used for screening fetal heart malformations due to its non-invasiveness, simple operation, and good reproducibility[7]. Two-Dimensional Speckle Tracking Echocardiography (TDSTE) is a real-time quantitative analysis of fetal myocardial tissue motion and deformation based on myocardial rotation angle, velocity and action cycle signals[8,9]. With the rapid development of medicine in recent years, the traditional static two-dimensional echocardiography has evolved to dynamic three and four-dimensional imaging. Compared with two-dimensional echocardiography, four-dimensional echocardiography allows a direct display of the structure, adjacency and spatial location of the fetal heart[10,11]. In addition, 4-dimensional technology shortens the fetal ultrasound exposure time, compensates for the shortcomings of 2-dimensional ultrasound and provides the advantages of easy operation and high safety in fetal congenital heart disease screening. To this end, the current research was performed to evaluate the diagnostic efficiency of four-dimensional echocardiography plus TDSTE in fetal congenital heart disease.

MATERIALS AND METHODS

Research design:

In this randomized controlled trial, pregnant women with fetal congenital heart malformations who underwent maternity examination in our hospital between January 2019 and December 2021 were recruited for eligibility assessment and 140 cases were eventually included. The eligible patients were assigned to receive either TDSTE (2-dimensional group) or TDSTE plus four-dimensional echocardiography (combined group) *via* random number table method in a 1:1 ratio, with 70 cases in each group. This study was conducted following the Declaration of Helsinki and all study participants voluntarily signed the consent form.

Inclusion and exclusion criteria:

Inclusion criteria: Pregnant women with congenital fetal heart malformation who underwent maternity examination in our hospital; all were diagnosed based on pathological or postnatal neonatal echocardiographic findings; participants had complete clinical data and were adult and singleton pregnancies.

Exclusion criteria: Maternal diseases such as heart failure; patients with mental abnormalities that prevent normal communication and clinical contraindications related to ultrasound examination.

Detection methods:

TDSTE: With the study participant in the left lateral recumbent position, TDSTE was performed using the S5-1 probe (1-5 MHz frequency) of the color ultrasound diagnostic instrument (LOGIQ S8, original registration number: State Arm Note Approval 20173231302, General Electric Medical Systems (China) Co. Images of the fetal apical two-chamber view, left apical long-axis view and four-chamber apical view were acquired during three consecutive cardiac cycles.

Four-dimensional echocardiography: With the study participant in a lying or lateral position, four-dimensional echocardiography was performed using a four-dimensional diagnostic ultrasound instrument (GE Voluson 730 Expert, United States of America (USA)) using a switched four-dimensional ultrasound probe (2.5-7 MHz frequency). Following the ALARA principle, image acquisition was performed based on data related to cardiac volumes, minimizing the number of acquisitions and scan time. The fetus was examined by 2-dimensional ultrasound and routine measurements were performed to examine three parts of the fetal heart, including the four chambers, the left and right ventricular outflow tract sections and the three-vessel plane. The four-dimensional volume sampling frame was used and the four-dimensional mode was enabled for the detection site using the surface smoothing mode with timely adjustment of the x-axis, y-axis and z-axis. Once a clear dynamic 3-dimensional image appeared on the screen, the specifics and parameters of each part of the fetus were obtained, photographed and stored by moving the probe. The data from the 4-dimensional images were analyzed to identify the presence of fetal diseases.

Outcome measures:

The findings of the two examination modalities were recorded, including Global Longitudinal Strain (GLS), mean peak Systolic Strain Rate (mSRs), mean peak late Diastolic Strain Rate (mSRa) for TDSTE and atrial septal anomalies, left heart dysplasia syndrome, right heart dysplasia syndrome, arterial system anomalies, cone stem anomalies and simple atrioventricular valve anomalies for four-dimensional echocardiography. The screening time (time required per image *vs.* per sample) was recorded and the results of data analysis were statistically compared between the two groups using pathological anatomy as the diagnostic criterion, and the diagnostic efficacy of the two groups was compared, including specificity, sensitivity and Jorden index.

Data analysis:

The software used was Statistical Package for the Social Sciences (SPSS) 26.0. Measurement data were expressed as (x±s) and tested using independent samples t-test. Count data were expressed as number of cases (%) and tested using Chi-square (χ^2) test. Statistical significance was indicated by $p<0.05$.

RESULTS AND DISCUSSION

Patients in the 2-dimensional group were 20-35 y (25.89±7.11) y old, weighed 58-85 kg (70.23±10.51) kg, had 21-38 w (25.18±4.91) w of gestation, with 57 primiparous and 13 pluriparous cases, 64 married, 6 unmarried and years of education in the range of 7-16 y (15.18±5.36) y. Patients in the combined group were 22-36 y (26.28±7.23) y old, weighed 56-84 kg (69.86±10.44) kg, had 21-38 w (25.01±5.14) w of gestation, with 59 primiparous and 11 pluriparous cases, 61 married, 9 unmarried and years of education in the range of 7-16 y (15.23±5.14) y. The two arms were well-balanced in baseline profiles ($p>0.05$) as shown in Table 1.

The GLS was (15.15±1.41), mSRs was (1.45±0.45) and mSRa was (-2.15±0.56) in the 2D group, and the GLS was (15.23±1.33), mSRs was (1.68±0.32), and mSRa was (-2.34±0.61) in the combined group. Four-dimensional echocardiography identified 32 cases of atrial septal abnormalities, 7 cases of left heart dysplasia syndrome, 6 cases of right heart dysplasia syndrome, 10 cases of arterial system abnormalities, 6 cases of cone stem abnormalities and 6 cases of simple atrioventricular valve abnormalities. The difference between the two groups in TDSTE was of no statistical significance ($p>0.05$) as shown in Table 2.

In the 2-dimensional group, 54 cases were diagnosed, and 16 cases were not diagnosed, with a diagnostic accuracy rate of 77.14 % and in the combined group, 67 cases were diagnosed, and 3 cases were not diagnosed, with a diagnostic accuracy rate of 95.71 %. Combined detection produced markedly higher diagnostic accuracy *vs.* single detection ($p<0.05$) as shown in Table 3.

TABLE 1: BASELINE PROFILES

		2-dimensional group	Combined group	t	p
n		70	70		
Age (year)	Range	20-35	22-36		
	Mean	25.89±7.11	26.28±7.23	0.322	0.741
Weight (kg)	Range	58-85	56-84		
	Mean	70.23±10.51	69.86±10.44	0.209	0.819
Gestational weeks	Range	21-38	21-38		
	Mean	25.18±4.91	25.01±5.14	0.2	0.841
Gravidity	Primiparous	57	5595		
	Pluriparous	13	11		
Marriage	Married	64	61		
	Unmarried	6	9		
Years of education	Range	7-16	7-16		
	Mean	15.18±5.36	15.23±5.14	0.056	0.991

TABLE 2: EXAMINATION RESULTS

		2-dimensional group	Combined group
n	-	70	70
Two-dimensional speckle tracking echocardiography	GLS	15.15±1.41	15.23±1.33
	mSRs	1.45±0.45	1.68±0.32
	mSRa	-2.15±0.56	-2.34±0.61
Four-dimensional echocardiography	Atrial septal abnormalities	-	32 (45.71)
	Hypoplastic left heart syndrome	-	7 (10.00)
	Right heart dysplasia syndrome	-	6 (8.57)
	Arterial system anomalies	-	10 (14.29)
	Cone stem anomalies	-	6 (8.57)
	Simple atrioventricular valve abnormalities	-	6 (8.57)

TABLE 3: DIAGNOSTIC EFFICIENCY

	2-dimensional group	Combined group	χ^2	p
n	70	70	-	-
Diagnosed	54	67	-	-
Undiagnosed	16	3	-	-
Diagnosis accuracy rate	77.14	95.71	10.291	<0.001

The time required for TDSTE was (1.21±0.56) per image and (9.45±2.54) per sample and the time required for four-dimensional echocardiography was (0.81±0.21) per image and (7.25±2.13) per sample. Four-dimensional echocardiography was associated with a significantly shorter disease screening time *vs.* TDSTE ($p<0.05$) as shown in Table 4.

The specificity and sensitivity of the 2-dimensional group were 86.45 % and 53.88 % and the specificity and sensitivity of the combined group were 94.15 % and 81.14 %. Hybrid detection provided higher specificity and sensitivity for the detection of fetal congenital heart disease *vs.* single TDSTE ($p<0.05$) as shown in Table 5.

The prevalence of congenital heart disease is about 7 %-8 % and about 140 000 to 160 000 children with congenital heart disease are born each year in China. Currently, complex congenital heart disease features difficult management and poor prognosis and most of the affected children suffer from severe physical defects, which causes a great burden to society and families[12,13]. Therefore, reasonable prenatal examination, early diagnosis and timely intervention are of great importance for the health of pregnant women and fetuses.

Ultrasound is currently a clinical approach for prenatal diagnosis of fetal congenital heart disease[14]. Two-dimensional ultrasound has been widely used for prenatal diagnosis, but misdiagnosis has also been reported. The results of the present study showed that four-dimensional echocardiography provided shorter screening time and higher diagnostic efficiency, specificity and sensitivity than two-dimensional speckle-tracking echocardiography. The results suggested that hybrid detection markedly enhances the accuracy and specificity of the diagnosis of congenital heart disease. Two-dimensional ultrasound is the most common and widely used examination method but only provides cross-sectional images of a certain part of the body. Previous studies suggest that the two-dimensional speckle tracking technique, based on two-dimensional grayscale imaging, selects a series of regions of interest from myocardial tissue and automatically tracks the position and motion of noisy spots in said regions of interest frame by frame according to tissue grayscale and heart rate cycle, thereby obtaining the strain rate and rotation angle of myocardial tissue motion independent of the direction of the acoustic beam and the angle between wall motion and overall cardiac motion. It provides a more objective method for evaluating myocardial function and more accurately reflects ventricular systolic and diastolic function by sensitively identifying abnormal myocardial segmental motion[9,15]. It is an echocardiographic technique used for deformation analysis of two-dimensional myocardial motion images, where individual "echo points" in the myocardial tissue are formed by reflection and scattering of small structures in the two-dimensional grayscale image below the incident echocardiographic wavelength. However, due to its high requirements for two-dimensional image quality and frame rate, it requires a clear endocardium to ensure the accuracy of tracking measurements. Sinus heart rate is necessary and the mean heart rate of patients requires to be essentially the same, as excessive heart rate variation reduces the reliability of the analysis results[16,17]. The diagnosis of prenatal complex congenital heart malformations is extremely challenging due to limitations in image resolution and detection techniques. The dynamic real-time display mode of four-dimensional echocardiography is akin to the traditional video recording mode, allowing retrospective analysis and processing, and has been applied in the prenatal diagnosis of fetal congenital heart disease with established efficiency. Chaoui *et al.* reported that the combination of the 4-dimensional cardiography technique, color Doppler ultrasound and power Doppler ultrasound to display the spatial relationship of fetal vessels is instrumental in the diagnosis of complex fetal vascular malformations. Moreover, its three-dimensional reconstruction, surface imaging and ultrasound tomography can directly visualize the cross-sectional area of the aorta and pulmonary arteries as well as the location of the atrioventricular valves, which contributes to the diagnosis of congenital cardiac malformations, pleural effusion and fetal diabetic cardiomyopathy. The findings were consistent with the current research results. Four-dimensional ultrasound, as a new diagnostic technique, provides a new method for the diagnosis of fetal malformations[7,18]. It provides clear three-dimensional images, especially surface imaging of facial malformations, allowing for more intuitive and accurate diagnosis[19]. The sensitivity, specificity and accuracy of four-dimensional ultrasound in diagnosing fetal abnormalities are higher than those of two-dimensional ultrasound by providing more diagnostic information. Four-dimensional ultrasound can rapidly comprehend abnormal fetal movements and provide a better understanding of fetal body features and physiological structures, three-dimensional shapes and positional relationships, thereby offering more accurate image information for the diagnosis of fetal congenital heart disease[19,20]. Four-dimensional echocardiography combined with TDSTE displays fetal heart structures in a multi-layered and multi-angle fashion. Four-dimensional reconstruction allows the use of different imaging modalities to display three-dimensional ultrasound images of the heart, enabling a detailed view of the fine structures of the fetal heart from different angles and revealing views unavailable through ultrasound in real-time. Thus, it reduces the reliance on experience in clinical diagnosis, effectively screens for fetal congenital heart disease, and improves the accuracy of detection results. The present clinical results demonstrated that four-dimensional echocardiography combined with TDSTE could significantly improve the diagnostic accuracy of prenatal diagnosis of fetal congenital heart disease.

TABLE 4: SCREENING TIME

	Two-dimensional speckle tracking echocardiography	Four-dimensional echocardiography	t	p
n	140	70	-	-
Time required per image (min)	1.21±0.56	0.81±0.21	5.596	<0.001
Time required per sample (min)	9.45±2.54	7.25±2.13	5.553	<0.001

TABLE 5: SENSITIVITY AND SPECIFICITY

	2-dimensional group	Combined group	χ^2	p
n	70	70	-	-
Specificity	86.45	94.15	5.987	<0.001
Sensitivity	53.88	81.14	12.569	<0.001

TDSTE is an accurate, reliable, sensitive and non-invasive new technique in the field of ultrasound to study myocardial motion and function, which provides more objective myocardial mechanical and myocardial deformation parameters for quantitative evaluation of local and overall myocardial function. TDSTE combined with four-dimensional echocardiography allows real-time observation of dynamic movements of human internal organs, multi-angle and multi-directional observation of intrauterine growth and development of the fetus, providing an accurate scientific basis for early diagnosis of fetal body surface anomalies and congenital heart disease.

The sample selection for this study was conducted using random sampling, and there may be selectivity bias in that the sampled samples are not representative of the parent population under study. Constrained by the scope of application of the intervention, the subjects selected for the study were all from the same center during the same period, with insufficient sampling costs, too geographically concentrated sampling, and insufficient representativeness, which may affect the extrapolation of experimental results to the aggregate to varying degrees. There is also a lack of existing clinical studies on this topic, with fewer references and insufficient depth of research. Future studies will expand the sample and modify the protocol to provide more references for future related diagnostic treatments.

Hybrid detection of four-dimensional echocardiography with TDSTE provides enhanced diagnostic efficiency and a higher detection rate for congenital heart disease *vs.* single detection. Compared with single detection, joint examination mode provides more accurate image information for the diagnosis of fetal congenital heart disease by understanding fetal heart structural abnormalities, fetal body surface features and physiological structures, three-dimensional shape and position relationships. Therefore, the combined examination contributes to guiding the early treatment of fetal congenital heart disease and improving the prognosis.

Conflict of interests:

The authors declared no conflict of interests.

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