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Clinical application of the quantitative fetal heart quantification in the evaluation of right heart function in fetuses with redundancy foramen ovale flap

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Abstract

Background To investigate the clinical value of fetal heart quantification (fetal HQ) in the evaluation of right ventricular size, morphology and cardiac function in fetuses with redundancy foramen ovale flap (RFOF).

Methods 31 fetuses diagnosed with RFOF through echocardiography from September 2021 to December 2023 were selected as the control group, and 62 healthy fetuses that matched the age and gestational period of the pregnant women in the RFOF group were chosen as the control group. Fetal HQ software provided by GE Voluson E10 was employed to automatically track endocardial parameters of the right ventricle in 24 segments.

Results The internal diameter of foramen ovale in RFOF group was significantly smaller than that of normal fetal diameter in control group, with statistical significance ($P < 0.05$). Comparing the morphological parameters of the fetuses in the RFOF group and the control group, there was no statistically significant difference in the GSI scores ($P > 0.05$), but the RV-LED of the fetuses in the RFOF group in the segments of 1–24 were higher than the fetuses in the normal control group (both $P < 0.05$), and the RV-SI was lower than that in the normal control group (all $P < 0.05$).

Conclusions The Fetal HQ technique enables accurate localisation of the site of the RFOF foetal lesion by rapid quantitative analysis of morphological and functional parameters of the right ventricle of the foetal heart.

Keywords Fetal heart quantification, Redundancy foramen ovale flap, Right ventricular function, Echocardiography

Background

The foramen ovale is an important physiological channel in the fetus, which carries oxygenated blood to the left cardiac system to supply the head, neck and upper limbs [1]. When the oval valve is redundant, the shunt from the right atrium into the left atrium is reduced, which also leads to obstruction of pulmonary venous return and reduced blood flow through the mitral valve into the left ventricle, leaving the left atrium in a low-pressure state, which further contributes to insufficient perfusion of the left heart, thus leading to an imbalance in the ratio of the left to right heart [2]. Previous studies have mostly reported on the overall ventricular shape in adults, but in recent years, with the advancement of ultrasonography, the study of cardiac function in the fetal heart has gradually been developed [3]. The aim of this study is to investigate the clinical value of using fetal HQ technique to assess the morphology of the right ventricle and cardiac

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function of the fetal heart in the case of RFOF, with the aim of providing a more accurate reference for early diagnosis, prenatal counselling, and prognostic treatment.

Methods

Thirty-one fetuses diagnosed as RFOF by fetal echocardiography were selected from September 2021 to December 2023 in Gansu Maternal and Child Health Hospital (Gansu Provincial Central Hospital), and 62 healthy fetuses matched with the RFOF group in terms of gestational week and age during the same period were selected as the control group. The age of the pregnant women was 20–41 years (average, 31.29 ± 3.75 years); and the gestational week of first detected was 20–40 weeks (average, 31.92 ± 5.05 weeks). All pregnant women attending the clinic signed an informed consent form for fetal echocardiography. Inclusion criteria: Single pregnancy with RFOF diagnosed by fetal echocardiography; Pregnant women are free from pregnancy complications and complications, etc.; There was no history of abnormal medication, pets or radiation exposure during pregnancy; There were no chromosomal abnormalities in the mother or foetus. Exclusion criteria: Twin or multiple pregnancies; The structural diseases of the heart include type A pulmonary arterial hypertension, severe coarctation and ankylosing spondylitis. Other cardiac conditions include arrhythmias and infections, such as pericarditis, as well as functional disorders of the heart, placental disorders and syndromic disorders; Unsatisfactory images due to the influence of thicker abdominal wall fat of pregnant women, fetus, etc.; Incomplete clinical information or missed visits.

Diagnostic criteria for oval valve redundancy: Overprojection of the foramen ovale flap into the left atrium exceeding at least 50% of the transverse diameter of the left atrium was RFOF [2, 4]. In this study, the ratio of foramen ovale flap diameter (FOFd) to left atrium diameter (LAd) ≥ 0.65 was defined as RFOF cases (Fig. 1).

GE Voluson E10 ultrasonic diagnostic instrument was used with a 3D volumetric probe RM6C with a frequency of 2 ~ 7 MHz and a belly convex probe C6-1 with a frequency of 1 ~ 6 MHz. Equipped with fetal HQ analysis software. The pregnant woman was asked to lie in the supine position and routine fetal 2D ultrasound and fetal echocardiography were performed. The four-chamber core section of the apex was taken to make the apex face the probe as far as possible, adjust the instrument conditions, optimize the image quality, strengthen the boundary between the ventricular cavity and the endocardial cavity, and store 2–3 s dynamic video at a frame rate of ≥ 80 Hz. The fetal HQ software was enabled for quantitative analysis of the fetal heart. The global sphericity index (GSI) was obtained from the ratio of the length to width diameter of the four-chamber heart section, and M-mode ultrasound combined with two-dimensional echocardiography was used to determine the timing of valve closure, with sampling points placed at the tricuspid valve-ventricular junction and the apical portion of the right ventricle, and the right ventricular endocardium was traced automatically by the software (Fig. 2). Fetal HQ divides the right ventricle into 24 segments (Fig. 3), and the software automatically calculates the quantitative data corresponding to each segment, with a Z-score defining – 2–2 as the normal range. All images were quality controlled and screened by two senior physicians.

SPSS 25 statistical software was used to analyse the data. Measurements that conformed to normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$), and t-tests were used to compare the two groups. Correlations between the parameters and GA were analysed

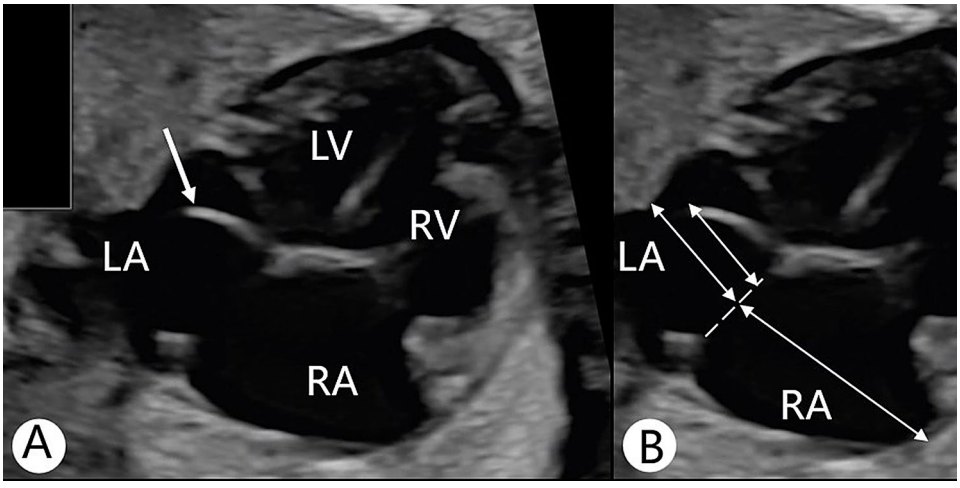

Fig. 1 Measurement of four-chamber incisional plane of fetus with long oval valve (one-way arrow shows long oval valve). LA: left atrial, RA: right atrial, LV: left ventricle, RV: right ventricle

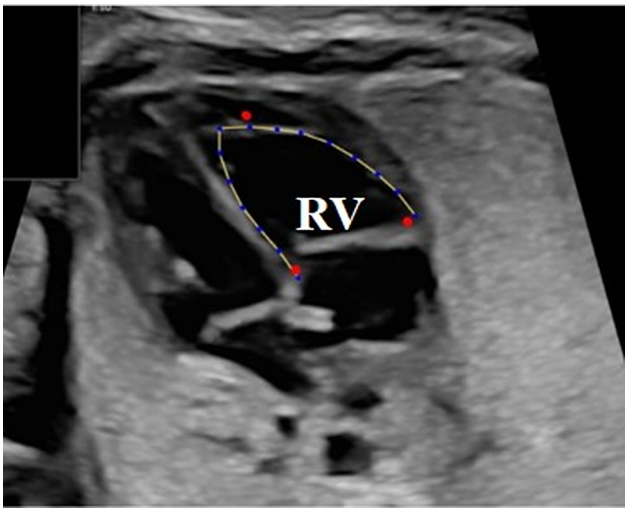

Fig. 2 Fetal right ventricular endocardial speck tracing under Fetal HQ

using Pearson correlation analysis. Differences were considered statistically significant at $P < 0.05$.

Results

This study included 31 cases in the RFOF group and 62 cases in the control group. The weeks of gestation detected in the RFOF group ranged from 24 to 39 weeks, with 5 cases detected in the middle trimester (all between 24 and 28 weeks) and 26 cases detected in the late trimester (≥ 28 weeks). Thirty-one fetuses in the RFOF group had varying degrees of oval valve redundancy and tricuspid regurgitation, including one with pulmonary valve atresia (type I), five with premature ventricular contractions, three with small amounts of pericardial effusion, one with a single umbilical artery (right branch missing), and one with hepatic hemangioendothelioma and choroidal malformation. There were no statistically significant differences between fetuses in the RFOF group and the control group in terms of maternal age, gestational week, 4CV LED, 4CV TWED, GSI parameters (all $P > 0.05$), but the internal diameter of the foramen ovale in the RFOF group was significantly smaller than that of the control

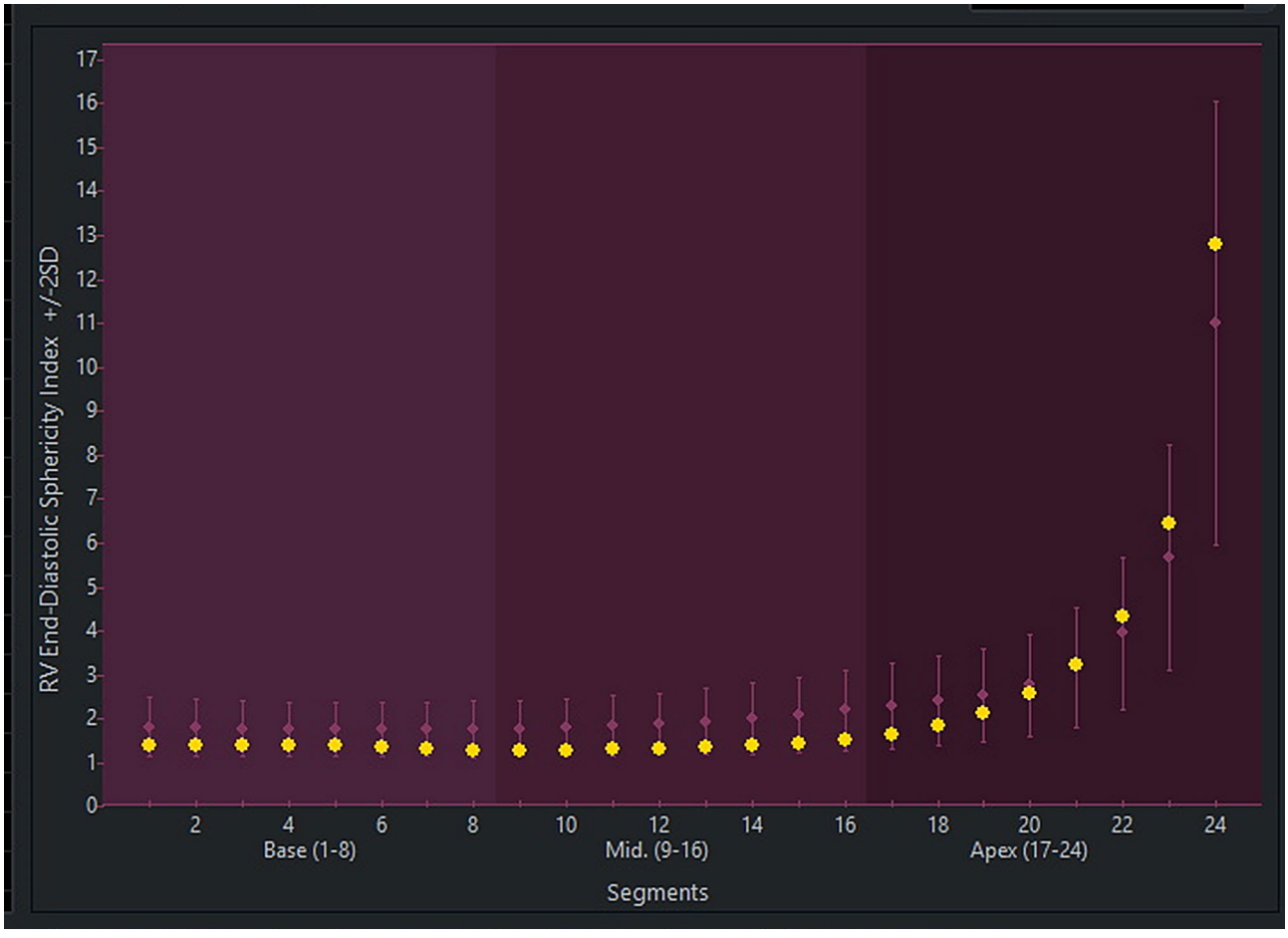

Fig. 3 Fetal right ventricular segment 24 SI with redundant oval valve

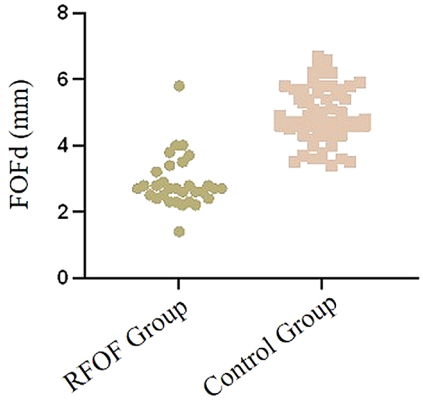

Fig. 4 Analysis of the difference between the fetus with redundant oval valves and the normal fetus

Table 1 Comparison of general clinical data of foetuses in the RFOF group and the control group ($\bar{x}\pm s$)

Variant	RFOF Group ($n=31$)	Control Group ($n=62$)	t-value	*p*-value
Age (year)	30.94 ± 4.74	31.53 ± 3.46	-0.654	0.515
Gestation week (week)	31.52 ± 3.97	31.58 ± 3.90	-0.074	0.941
FOFd (mm)	2.88 ± 0.79	4.94 ± 0.85	-11.309	<0.001*
4CV LED(mm)	41.86 ± 5.80	42.42 ± 5.86	-0.438	0.663
4CV TWED(mm)	34.06 ± 4.85	34.08 ± 5.24	-0.021	0.983

Abbreviations: FOFd: foramen ovale flap diameter, 4CV LED: four-chambered length end-diastolic, 4CV TWED: four-chambered transverse width end-diastolic

group, and the difference was statistically significant ($P < 0.001$) (Fig. 4; Table 1).

Fetal HQ automatically measures GSI and fetal cardiac morphologic indices such as right ventricular 24-segment LED and SI by speckle tracking technology in order to quantitatively assess the morphological changes in the right ventricle of the RFOF fetal heart. In this study, the fetal HQ technique was used to compare the RFOF group with the control group, and it was found that there was no statistically significant difference in GSI between the two groups of foetuses ($P > 0.05$), but when analysing the right ventricular 24-segment analysis, it was found that the SI of the right ventricle in the RFOF group was lower than that of the normal control group in the RV 24-segment analysis ($P < 0.05$), which suggests that the right ventricle of the RFOF foetus is more spherical in shape (Table 2).

Fetal HQ allows for a more accurate quantitative evaluation of changes in fetal cardiac function, in addition to assessing the size and morphology of the fetal heart. This study mainly assessed 24-segment fractional shortening (FS) in the right ventricle of the fetus in the two groups, and the results showed no statistical difference between the two groups (all $P < 0.05$).

All fetuses were followed up to 42 days postpartum. All normal fetuses were healthy. Of the 31 fetuses with oval valve redundancy, one was diagnosed with pulmonary atresia (type I) with oval valve redundancy combined with massive tricuspid regurgitation, and the other with oval valve redundancy combined with massive tricuspid regurgitation, both of which resulted in a significant enlargement of the right atrium. The pregnant woman and her family consulted a prenatal diagnostician, and after a comprehensive assessment of the poor outcome of the fetal pregnancy, the decision was made to terminate the pregnancy. The remaining 29 fetuses chose to continue the pregnancy, of which 18 were delivered by surgical cesarean section and 11 by normal delivery. The echocardiographic assessment of children at 42 days, 6 months and 1 year of age has been undertaken. We found that cardiac examination in 26 children showed an unclosed foramen ovale, with a small amount of tricuspid regurgitation in 9 cases, and there were no other obvious signs of abnormality; the remaining 3 cases were under follow-up observation (1 case with a closed foramen ovale and an enlarged right atrium; 1 case with a small amount of pericardial effusion and hepatic hemangioendothelioma; and 1 case with episodic cardiac arrhythmia).

Discussion

The foramen ovale is a specialized anatomical structure during embryonic development, through which most of the highly oxygenated blood from the mother enters the right atrium and then flows directly into the left heart to participate in the circulation of body fluids, which is the only pathway supplying the left heart and upper body of the fetus [5]. The long foramen ovale valve will lead to the shunt flow from the right atrium into the left atrium, and the foramen ovale valve that expands into the left atrium will also obstruct the diastolic pulmonary venous return, which in the past led to the disproportion between the right and left fetal heart, abnormal heart shape and function, and even intrauterine fetal death [2]. The degree of redundancy of the foramen ovale is closely related to the time of closure of the foramen ovale flap after birth of the fetus; the longer the foramen ovale flap, the later the time of closure [6]. Furthermore, the presence of aneurysmal for amen oval has been identified as a risk factor for type II atrial septal defects (ASD II) in postpartum newborns. Therefore, early recognition of oval valve overgrowth can help monitor changes in fetal cardiac function and provide guidance value for prenatal intervention, prognosis, and postnatal treatment.

Traditional evaluation methods of fetal heart function include blood flow spectrum detection, tricuspid annular plane systolic excursion (TAPSE), Tei index, etc [7, 8]. but these routine assessments have limited sex on fetal heart shape and myocardial deformation. With the

Table 2 Comparison of fetal right ventricular parameters in RFOF and control groups ($\bar{x}$±s)

	Seg-1	Seg-2	Seg-3	Seg-4	Seg-5	Seg-6	Seg-7	Seg-8	Seg-9
RFOF Group RV-LED(mm)	13.83±2.41	13.91±2.29	13.98±2.19	14.03±2.12	14.03±2.07	13.98±2.02	13.87±1.98	13.69±1.97	13.44±1.97
Control Group RV-LED(mm)	11.81±2.51	11.82±2.50	11.84±2.52	11.84±2.55	11.80±2.56	11.71±2.53	11.57±2.49	11.40±2.43	11.18±2.38
t-value	3.716	3.895	4.02	4.12	4.217	4.345	4.469	4.552	4.574
p-value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
RFOF Group RV-SI	1.27±0.30	1.25±0.28	1.24±0.28	1.24±0.28	1.25±0.25	1.26±0.28	1.24±0.28	1.28±0.26	1.29±0.27
Control Group RV-SI	1.47±0.45	1.46±0.45	1.46±0.45	1.46±0.44	1.47±0.44	1.48±0.44	1.49±0.44	1.51±0.44	1.54±0.45
t-value	-2.282	-2.387	-2.543	-2.527	-2.518	-2.538	-2.883	-2.731	-2.85
p-value	0.025*	0.019*	0.013*	0.013*	0.014*	0.013*	0.005*	0.008*	0.005*
	Seg-10	**Seg-11**	**Seg-12**	**Seg-13**	**Seg-14**	**Seg-15**	**Seg-16**	**Seg-17**	**Seg-18**
RFOF Group RV-LED(mm)	13.13±1.96	12.76±1.94	12.34±1.91	11.88±1.86	11.01±1.65	10.86±1.75	10.28±1.69	9.67±1.61	9.00±1.53
Control Group RV-LED(mm)	10.92±2.33	10.61±2.29	10.26±2.24	9.87±2.20	9.45±2.15	8.96±2.06	8.45±1.97	7.90±1.85	7.31±1.71
t-value	4.545	4.486	4.414	4.361	4.374	4.389	4.448	4.54	4.643
p-value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
RFOF Group RV-SI	1.31±0.29	1.39±0.31	1.44±0.33	1.51±0.35	1.58±0.39	1.67±0.43	1.77±0.46	1.88±0.47	2.02±0.47
Control Group RV-SI	1.58±0.48	1.63±0.51	1.70±0.56	1.77±0.61	1.86±0.67	1.97±0.74	2.10±0.80	2.24±0.86	2.42±0.92
t-value	-2.862	-2.417	-2.351	-2.194	-2.171	-2.059	-2.104	-2.19	-2.235
p-value	0.005*	0.018*	0.021*	0.031*	0.033*	0.042*	0.038*	0.031*	0.028*
	Seg-19	**Seg-20**	**Seg-21**	**Seg-22**	**Seg-23**	**Seg-24**			
RFOF Group RV-LED(mm)	8.25±1.47	7.36±1.45	6.28±1.38	4.96±1.19	3.41±0.87	1.75±0.46			
Control Group RV-LED(mm)	6.65±1.57	5.92±1.47	5.04±1.33	3.96±1.11	2.75±0.80	1.39±0.42			
t-value	4.715	4.477	4.209	3.977	3.667	3.728			
p-value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*			
RFOF Group RV-SI	2.22±0.46	2.52±0.45	2.98±0.50	3.82±0.67	5.39±0.83	10.87±1.93			
Control Group RV-SI	2.64±0.99	2.97±1.11	3.51±1.31	4.48±1.69	6.52±2.47	12.82±4.89			
t-value	-2.256	-2.206	-2.157	-2.096	-2.48	-2.133			
p-value	0.026*	0.030*	0.034*	0.039*	0.015*	0.036*			

advancement of ultrasound technology, speckle tracking imaging has become increasingly sophisticated, pioneering its application in adult and pediatric cardiac evaluation [9, 10], and some scholars have applied it to the fetus. In recent years, the fetal heart has received increasing attention, and Devore et al. have developed a software specifically for fetal heart assessment, fetal heart quantification (fetal HQ) [11]. The software assessed fetal heart size, shape, and function by capturing four-chamber heart sections and automatically tracking the endocardium over the full cardiac cycle. Compared with traditional technology, fetal HQ is quick and easy to use, offers multiple quantitative indicators, and is reproducible. It has great potential in the assessment of fetal development and cardiovascular complications [12], and this technique is currently playing an increasingly important role in the assessment of fetal cardiac function [13, 14].

Currently, domestic and international researchers have applied this technique in the study of fetal cardiac function abnormalities, including gestational diabetes mellitus, gestational hypertension, fetal growth restriction, narrowing of the aortic arch, and arterial ductus arteriosus, etc [4]. Through the study of these diseases, fetal HQ technology has been found to be critical in identifying small changes in the heart to aid in effective clinical intervention and management. SI can be used as a quantitative index to assess the shape and size of fetal ventricles, which can help to identify changes in the shape of the ventricles in fetal cardiac structures at an early stage [15]. The results of this study showed no statistically significant difference between the GSI of RFOF fetuses and normal fetuses, with GSI values of 1.24 ± 0.13 in RFOF fetuses and 1.25 ± 0.09 in normal fetuses, suggesting that even though the redundancy of the oval valve caused uneven distribution of left and right cardiac blood flow in RFOF fetuses, it did not cause any alteration of the overall cardiac morphology. However, the results showed that the internal diameter of the foramen ovale

in RFOF fetuses was significantly smaller than that in normal fetuses, and the comparison of the two was statistically different. The reason for this may be that in the case of redundant foramen ovale flap, the excessively long foramen ovale flap obscures the blood flow channel of the foramen ovale, and the poor filling of the foramen ovale results in the narrowing of the internal diameter of the foramen ovale. Comparison of right ventricular indices between RFOF fetuses and normal fetuses revealed that the right ventricular transverse diameter of all 24 segments of the right ventricle in RFOF fetuses was greater than that of normal fetuses, whereas the SI was smaller than that of normal fetuses, indicating that fetuses in the RFOF group had a significant right-centerricular predominance, suggesting that it may be due to the increased volume of blood from the right atrium entering the right ventricle, the transverse width of the right ventricle, and the basal-tapering length of the right ventricle, which makes the RV more spherical and pushes the ventricular septum convexly toward the left ventricular side and thus the left ventricle, resulting in a disproportionate ratio of right to left ventricles. The results of all these studies show that the size and shape of the right ventricle are altered in the presence of oval valve redundancy.

Previous studies have shown that decreased cardiac function is closely associated with ventricular remodeling, such as change in ventricular shape (from elliptical to spherical), increased end-diastolic volume, and decreased ventricular function [16, 17]. In this study, the changes of cardiac function were evaluated according to the FS of the two groups of fetuses, and the results showed that no significant abnormalities in right ventricular transverse contractility were seen in the RFOF fetuses. The authors may have been motivated by the fact that RFOF is usually detected in late pregnancy and normal fetuses in late pregnancy also show right heart dominance, and it has been previously reported that the fetal heart is more malleable compared to postnatal life and may be able to adapt more easily to changes in cardiac morphology, whereas alterations in ventricular size and shape may be a compensatory mechanism to improve stroke volume, implying that ventricular dilatation is a response to volume overload [18]. Since the development of all fetal cardiovascular structures is highly dependent on adequate blood flow and sufficient pressure for growth during the fetal period, right heart blood volume and left heart blood volume inevitably result in a disproportionate ratio of the left and right ventricles, hypoplastic aorta, and, in most severe cases, reversed blood flow through the narrowed isthmus of the aorta [19]. The 31 RFOF fetuses in this study showed aortic stenosis or narrowing of the aortic arch in 2 cases, left and right heart disproportion in 9 cases, and reversal of blood flow in the aortic isthmus in 1 case. In addition, it has been shown that in RFOF fetuses, the prevalence of restricted blood flow to the foramen ovale is 22% [20]. In this study, we found 25 cases of restriction of blood flow at the foramen ovale and 2 cases of fetal arrhythmias.

In conclusion, this study verified the feasibility and accuracy of this technique in clinical application by affecting the morphology and function of the right ventricular heart in RFOF fetuses. Applying the multi-indicator measurement parameters provided by fetal HQ technology can help us to determine the changes in the shape of the right ventricle and cardiac function of the RFOF fetus at an early stage, which can provide an important reference value for clinical prenatal interventions, prognosis and postnatal treatment.

Abbreviations

fetal HQ	Fetal heart quantification
RFOF	Redundancy foramen ovale flap
FOFd	Foramen ovale flap diameter
GSI	Global sphericity index

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Not applicable.

Author contributions
XS and TL carried out image acquisition and drafted the manuscript. AW andHT participated in the design of the study and performed the image analysis. QY and SC analyzed the patient data and examined the fetues. All authors read and approved the final manuscript.

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Data availability
The data and material in the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted according to the tenets of the Declaration of Helsinki. Informed consent was obtained from each patient. The study protocol was approved by the Medical Ethics Committee of Gansu Provincial Maternity and Child-care Hospital (Approval number 2023–54). All experiments were performed in accordance with relevant guidelines and regulations.

Consent for publication
The pregnant mothers provided their written informed consent and related images was obtained from the mother of the fetues.

Competing interests
The authors declare no competing interests.

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