Review Article

Fetal Speckle Tracking Echocardiography: A Comparison Between Fetuses with Normal Heart and Those With Heart Disease

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Abstract

Objective: The aim of our study was to compare left ventricular function in normal fetal hearts and those with cardiac abnormalities using 2D and 4D e-STIC approach.

Methods: We recruited 63 fetuses between 20- and 40- weeks, including twenty-nine affected by heart disease. All measurements were performed by two sonographers experienced in fetal echocardiography. We compared different parameters obtained by 2-dimensional and 4D e-STIC method in normal fetal hearts and those with cardiac defects. We focused on left ventricular global strain, left ventricular ejection fraction, left ventricular length and area in end-systole and end-diastole, and left ventricular fractional area change. Differences between categorical variables were analyzed by using Chi-Quadro Test, while continuous variables by one-way ANOVA Test.

Results: Firstly, no differences were proved between healthy and affected fetuses, regardless of the applied technique. Similarly, fetal strain values did not differ between the affected fetuses distinguished according to the kind of pathology.

Conclusion: In our cohort, 2D and 4D e-STIC imaging techniques have shown similar results for each parameter. We did not find differences between healthy fetuses and those with heart disease because congenital heart disease included did not affect left ventricular systolic function.

Keywords: Echocardiography; Fetal echocardiography; Speckle tracking; Strain; STIC

Introduction

Echocardiography is the most common tool used to diagnose congenital heart disease. Recently, 2-dimensional speckle tracking echocardiography (STE) has been introduced to investigate cardiac function, identifying the movement of endocardium during the cardiac cycle [1]. STE has been used to study segmental and global cardiac function, calculating velocities and deformation parameters such as longitudinal, radial and circumferential strain and strain rate, which are used to evaluate the myocardial function from an objective and quantitative point of view [2-4]. Moreover, 2D speckle tracking is independent from the heart orientation to the ultrasound beam [5-7]. In addition, thanks to the semiautomated software, it has better intra-observer and inter-observer reproducibility than the other techniques commonly used to evaluate cardiac function [3]. STE is currently applied both in adult and pediatric patients to evaluate ischemic heart disease, left ventricular diastolic dysfunction, myocardial mechanics, cardiomyopathy, vascular disease, and myocardial dysfunction in patients undergoing chemotherapy. Even if it has not yet been validated in the evaluation

of fetal cardiac dysfunction, it has already been used to measure myocardial deformation in twin-twin transfusion syndrome, fetal cardiomyopathies and structural heart diseases, gestational diabetes, and intrauterine growth restriction [9].

Although there have been differences in findings, STE is considered as an important tool for fetal specialists. However, several issues currently limit its use [8], especially regarding frame-rate and spatial resolution [9-14]. Recently, three-dimensional (3D) STE has been introduced to overwhelm B-mode imaging limitations. Previous studies proved that four-dimensional (4D) ultrasound technologies, such as spatio-temporal image correlation (STIC), facilitate examination of fetal cardiac images. However, obtaining diagnostic volumes could be limited by fetal movements. Standard mechanical probes allow acquisition of a STIC volume of good quality in 7.5-15 s [15-17]. 4D electronic probes improved image resolution and decreased image artifacts. Electronic STIC acquisition stitches together subvolumes resulting in a higher resolution real time image and in a faster technique [18,19]. The aim of our study was to compare left ventricular function in normal fetal hearts and those with cardiac abnormalities, using 2D STE and 4D e-STIC approach.

Methods and Materials

Population

This prospective study included fetuses between 20- and 40-weeks' gestation. Thirty-four control fetuses with accurate first or second trimester dating US exams were included. These fetuses were free of malformations or growth disturbances at the time of the inclusion and were referred to our clinic for second and third trimester ultrasound exams. Twenty-nine fetuses with congenital heart disease have been selected among fetuses evaluated in the fetal echocardiography clinic. The malformations were as follows: tetralogy of Fallot, ventricular septal defects, transposition of great arteries, dysplasia of tricuspid associated with pulmonary insufficiency, cardiomegaly with biventricular hypertrophy, aortic valve stenosis, aneurysm right atrium and cardiomyopathy of left ventricular with no-compacted myocardium.

Table 1a: fetal cardiac abnormalities split in 4 sub-groups: 1a (left heart disease), 1b (right heart disease), 1c (transposition of the great arteries), 1d (others). This division was used in the second phase of our study.

Fetal cardiac abnormalities (n=29)	
Group 1a: Left heart disease (n=11)	• Ventricular septal defect with Aortic valve dysplasia
	• Ventricular septal defect (n=3)
	• Interrupted aortic arch with hypoplastic ascending aorta and multiple ventricular septal defects
	• Ventricular septal defect with coarctation of aorta
	• Multiple ventricular septal defects
	• Inlet ventricular septal defects with multiple ventricular septal defects
	• Aortic valve stenosis with bicuspid aortic valve
	• Severe left ventricular noncompaction with ventricular septal defect and tricuspid valve dysplasia Ebstein-like
	• Dilated left ventricle with ventricular septal defect
Group 1b: Right heart disease (n=5)	• Tricuspid Valve Dysplasia (Non-Ebstein) with pulmonary atresia
	• Tetralogy of Fallot with pulmonary valve stenosis
	• Tetralogy of Fallot (n=2)
	• Double outlet right ventricle
Group 1c: Transposition of great arteries (n=7)	• Transposition of great arteries with ventricular septal defects (n=3)
	• Transposition of great arteries (n=3)
	• Transposition of great arteries with aneurysmatic patent foramen ovale
Group 1d: Others (n=6)	• Atrioventricular block
	• Cardiomegaly with biventricular hypertrophy and pericardial effusion
	• Neoformation in right atrium
	• Echogenic foci within the left ventricle
	• Atrial flutter
	• Aneurysmatic right atrium

Our study consisted of two phases: in the first one, fetuses have been divided in two groups (group 0: normal heart, group 1:congenital heart disease), while in the second phase fetuses affected by congenital heart disease have been split into 4 sub-groups (group 1a: left heart disease, group 1b: right heart disease, group 1c: transposition of the great arteries and group 1d: others) (Table 1a).

All measurements on healthy and affected fetuses were performed by two sonographers experienced in fetal echocardiography (A.P., A.B.).

Image acquisition and analysis

Two-dimensional images of the 4-chambers were acquired using a RM6C or EM6C transducer of the Voluson E10 US system (GE Healthcare, Milwaukee, WI). Three second cine clips of the 4-chambers view were obtained and stored as Digital Imaging and Communications in Medicine files and exported to an offline database. E-STIC volumes were acquired using an electronic 4D probe, EM6C, using the option maximal quality. Once the 2D images and 4D volumes of the 4-chamber view were obtained and stored, they were examined using fetalHQ software (GE Healthcare; Zipf, Austria) using criteria that have been previously described [5,15,18, 20-22]. Using the equation of Hadlock et al, estimated fetal weight (computing the measurements of the biparietal diameter, head circumference, abdominal circumference, and femur length) was expressed using z-score for each fetus [23,24]. At the end of the analysis, raw data were exported to an ASCII text file, later imported into an excel spreadsheet. In this study we focused on left ventricular global strain (GS), left ventricular ejection fraction (EF), left ventricular length and area in end-systole (ESL and ESA) and end-diastole (EDL and EDA), and left ventricular fractional area change (FAC).

Ethics

Each patient of the study signed a consent form at recruitment. The study protocol was approved by the local Ethics Committee of Sant' Orsola-Malpighi Hospital and a consent form signed at recruitment was obtained from each eligible patient (575/2018/Oss/AOUBo). The study protocol conforms to the ethical guidelines of the "World Medical Association (WMA) Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964 and amended by the 59th WMA General Assembly, Seoul, South Korea, October 2008.

Statistics

Categorical variables were expressed as percentage, while continuous variables were expressed as mean ± standard deviation if they are normally distributed. Differences between categorical variables were analyzed by using Chi-Quadro Test, while continuous variables by one-way ANOVA Test. A p-value lesser than 0,05 was considered statistically significative. All the analyses were done through STATA/IC 15.1

Result

The study included 62 fetuses recruited between October 2018 and May 2019, 34 with normal heart and 29 affected by congenital heart disease. Mean gestational age was 29,68 weeks±4,99 days and mean z-score estimated fetal weight was 0,24±1,26. 2D-images have been obtained in 62 fetuses, while the 4D images by STIC in 59 cases.

First phase

The population was homogeneously distributed in the mentioned groups. No differences were found between the groups in regard to gestational age (GA 29,34 ± 4,63 vs 30,09 ± 5,44) and estimated fetal weight (EFW 0,25 ± 0,22 vs 0,22 ± 0,31) at the time of examination (Table 1b). In Table 2 are summarized the measured values obtained with 2D and 4D e-STIC techniques. Compared to normal fetuses using 2D imaging, there was no statistically difference of EF, ESL, ESA, EDL, EDA, FAC, GS. There were not found any significantly different between the two groups of EF, ESL, ESA, EDL, EDA, FAC and GS obtained with 4D e-STIC.

Table 1b: gestational ages (expressed in weeks) and estimated fetal weight (expressed in z-score) of the two groups. Values are expressed as mean ± SD. Group 0 includes fetuses with normal heart. Group 1 includes fetuses with congenital heart disease. (G DAYS gestational age in days; G WEEKS gestational age in weeks, EFW estimated fetal weight).

	GROUP	MEAN±SD	IC 95%	P value
G WEEKS	0	29,34±4,63	27,72 - 30,95	0,552
	1	30,09±5,44	28,02 - 32,17	
EFW z-score	0	0,25±0,22	-0,20 - 0,70	0,945
	1	0,22±0,31	-0,45 - 0,90	

Table 2: Summary table of the first phase of the study. 0: fetuses with normal heart. 1: fetuses affected by congenital heart disease. Values are expressed as mean ± SD. EF: ejection fraction. ESL: end-systole left ventricular length. ESA: end-systole left ventricular area. EDL: end-diastole left ventricular length. EDA: end-diastole left ventricular area. FAC: fractional area change. GS: longitudinal global strain. STIC: images acquired using an electronic 4D probe. 2D: 2D images.

	GROUP	NUMBER OF PATIENT	MEAN±DS	ICC 95%	P-Value
EF STIC	0	34	61,73±9,37	58,45 65,00	0,762
	1	25	60,70±16,55	53,86 67,53	
EF 2D	0	34	59,58±9,78	55,86 62,69	0,872
	1	28	59,71±11,42	55,28 64,15	
ESL STIC	0	34	1,60±0,37	1,47 1,73	0,272
	1	25	1,48±0,41	1,31 1,65	

ESL 2D	0	34	1,57±0,34	1,45 1,70	0,537
	1	28	1,63±0,37	1,49 1,78	
ESA STIC	0	34	0,97±0,43	0,82 1,12	0,431
	1	25	0,88±0,40	0,71 1,05	
ESA 2D	0	34	0,91±0,38	0,77 1,04	0,361
	1	28	1,01±0,45	0,83 1,18	
EDL STIC	0	34	1,99±0,39	1,85 2,12	0,589
	1	25	1,92±0,47	1,73 2,12	
EDL 2D	0	34	1,93±0,36	1,81 2,06	0,144
	1	28	2,09±0,48	1,91 2,28	
EDA STIC	0	34	1,75±0,62	1,53 1,97	0,768
	1	25	1,70±0,73	1,39 2,00	
EDA 2D	0	34	1,60±0,57	1,40 1,80	0,169
	1	28	1,84±0,77	1,54 2,14	
FAC STIC	0	34	46,13±8,51	43,1 49,102	0,529
	1	25	47,62±9,60	43,66 51,59	
FAC 2D	0	34	44,08±8,79	41,01 47,15	0,723
	1	28	44,89±8,96	41,41 48,36	
GS% STIC	0	34	-22,09±6,07	-24,21 -19,97	0,173
	1	25	-24,41±6,76	-27,20 -21,61	
GS% 2D	0	34	-20,19±6,74	-22,55 -17,84	0,147
	1	28	-22,87±7,58	-25,81 -19,93	

Second phase

We divided the group 1 in 4 subgroups: group 1a, left heart disease (11 patients), group 1b, right heart disease (5 patients), group 1c, transposition of the great arteries (7 patients) and group 1d, others (6 patients with other cardiac diseases). Group 0 included 34 fetuses with normal heart. According to the value of gestational age (GA) and estimated fetal weight (EFW), the population was equally distributed in the mentioned groups (Table 3).

Table 3: gestational ages (expressed in weeks) and estimated fetal weight (expressed in z-score) of the five groups. 0=normal heart; 1a= left heart disease;1b=right heart disease; 1c=transposition of the great arteries; 1d=others.

	0	1a	1b	1c	1d	p-value
GA WEEKS	29,34±4,63	27,74±5,62	31,2±5,72	31,20±5,88	32,21±3,81	0,352
EFW z-score	0,25±1,30	0,31±1,17	-1,21±2,14	0,36±0,21	0,70±1,40	0,541

Table 4: Summary table of the second phase of the study. 0= normal heart; 1=left heart disease, 2: right heart disease; 3=transposition of the great arteries; 4=others. EF: ejection fraction. ESL: end-systole left ventricular length. ESA: end-systole left ventricular area. EDL: end-diastole left ventricular length. EDA: end-diastole left ventricular area. FAC: fractional area change. GS: longitudinal global strain. STIC: images acquired using an electronic 4D probe. 2D: 2D images.

Strain parameters	0 N=34	1 N=9	2 N=5	3 N=6	4 N=5	P-value
ESL STIC	1,60±0,37	1,39±0,37	1,39±0,38	1,49±0,42	1,75±0,51	0,362
ESA STIC	0,97±0,43	0,77±0,27	0,77±0,35	0,82±0,36	1,25±0,56	0,232
EDL STIC	1,99±0,39	1,82±0,49	1,79±0,44	1,90±0,42	2,29±0,50	0,292
EDA STIC	1,75±0,62	1,49± 0,54	1,44±0,50	1,61±0,72	2,42±0,92	0,09
FAC STIC	46,13±8,51	47,16±9,05	46,47±7,78	48,11±10,90	49,04±13,23	0,960
GS% STIC	-22,09±6,07	-26,06±7,5	-22,33±5,95	-22,29±6,044	-26,04±7,70	0,420
EF STIC	61,73±9,37	57,67±13.42	60,67±7,55	62,89±12,89	63,55±15,64	0,913
Strain parameters	0 N=34	1 N=11	2 N=5	3 N=6	4 N=6	P-value
ESL 2D	1,57±0,34	1,46±0,34	1,57±0,30	1,76±0,44	1,88±0,30	0,158
ESA 2D	0,91±0,38	0,87±0,38	0,86±0,45	1,09±0,54	1,30±0,43	0,200

EDL 2D	1,93±0,36	1,94±0,43	1,91±0,59	2,18±0,54	2,44±0,30	0,06
EDA 2D	1,69±0,57	1,67±0,73	1,47±0,67	1,97±0,97	2,32±0,60	0,117
FAC 2D	44,08±8,79	47,23±10,79	40,59±11,52	44,39±3,67	44,67±7,08	0,726
GS % 2D	-20,19±6,74	-25,78±8,48	-18,99±10,48	-20,67±3,62	-22,95±5,06	0,204
EF 2D	59,28±9,78	62,45±13,50	55,08±14,08	59,53±6,97	58,73±9,78	0,782

Table 4 summarizes the measurements obtained with both techniques. As in the first phase, the values of ESL, ESA, EDL, EDA, FAC, EF and GS acquired with 2D technique proved no significative differences between the five groups. Furthermore, there were not any statistically difference between five groups of ESL, ESA, EDL, EDA, FAC, EF and GS obtained with 4D e-STIC technique.

Discussion

This is the first study evaluating fetal left ventricular function by means of 2D and 4D e-STIC speckle-tracking echocardiography. We analyzed and compared several cardiac function parameters in normal fetal hearts and those with cardiac abnormalities. Speckle tracking is a semiautomated process, based on the tracking of 'speckles', conceptualized as small myocardial fingerprints, generated by ultrasound-myocardial tissue interactions during cardiac cycle. Specific algorithms allow to evaluate ventricular function [15]. Although 2D-speckle tracking is now considered equal or superior to Doppler techniques [12], thanks to its angle independency, it has several limitations [6,25,26]. The small size of the fetal heart, fetal movements and maternal breathing may affect the image resolution and the quality of the small tracking region. Trying to overcome its limits, recently, some authors experimented 3D approach to fetal speckle tracking echocardiography [27,28]. Our group had already outlined that 4D e-STIC technique can obtain optimal fetal heart volume in more than 90% of cases within the time frame of a standard examination of fetal anatomy [18,19,29].

Aiming to test these techniques to fetal heart abnormalities, we compared different parameters obtained by 2D and 4D e-STIC method in normal fetal hearts and those with cardiac defects. As we expected thanks to recent literature results, we did not find differences between the analyzed groups [5,30] because congenital heart diseases included did not affect left ventricular systolic function. However, post-natal test on a fetus affected by severe left ventricular noncompaction showed a significative low longitudinal strain (-13,9%) similarly to the value obtained during the fetal scan (-15,05%). Different pathophysiology lie under different cardiac abnormalities. The heterogeneity and complexity of cardiac abnormalities can complicate speckle tracking analysis and its interpretation, because the size of ventricular chambers can differ between a cardiac heart defect and another. This technical problem can be added to the uncertainty about angle independency of STE. Furthermore, regarding the acquisition rate, the frame rate is dependent on the angle and depth used for the acquisition [15], but no standards have been established yet to ensure the speckles can be tracked throughout the cardiac cycle. In our study we used high frame rates in order to optimize the resolution.

STE is a well-known modality in pediatric and adult echocardiography to follow changes in ejection fraction in patients with cardiomyopathy and to understand the kind of ventricular disfunction [8]. Even if it is not a routine clinical test in fetal cardiology, STE has the potential to improve our understanding on fetal cardiac function. Firstly, it could lead to the early detection of cardiac disfunction in several clinical conditions, such as structural defects, cardiomyopathies and risky diseases like Parvovirus B19 infection [31]. Moreover, we believe that STE will be a useful tool to compute the prognosis of affected and supposedly affected fetuses, such as DeVore et al had recently proved in a cohort of 108 fetuses with suspected prenatal diagnosis of aortic coarctation [32]. Nevertheless, published studies make comparison between healthy and affected fetus difficult and the results are not homogeneous [8]. There is still a lack of normal values for fetal systolic and diastolic function through gestation [33]. Moreover, the heterogeneity and complexity of cardiac abnormalities can complicate speckle tracking analysis and its interpretation [8]. We believe that this study provides an interesting approach to fetal speckle tracking echocardiography introducing the innovative 4D e-STIC method for cardiac abnormalities research. In our cohort, 2D and 4D e-STIC imaging techniques have shown similar results for each parameter. We believe that this approach will make STE more feasible in the future.

Conclusion

The main limitation of this study is the requirement of specialized software and an electronic probe to simultaneously calculate cardiac function parameters using 2D and 4D e-STIC approach. The small number of CHD group might have limited the analysis. We need a larger cohort for a better understanding of the correlation between the analyzed parameters and fetal cardiac malformations. Moreover, we acknowledge that further studies on healthy fetuses and those with congenital heart defects will be required to test feasibility and reproducibility of this new imaging technique.

Acknowledgement

None.

Conflict of Interest

No conflict of interest.

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