How automated techniques ease functional assessment of the fetal heart: applicability of two-dimensional speckle-tracking echocardiography for comprehensive analysis of global and segmental cardiac deformation using fetalHQ®

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May 05, 2024

Abstract

Background Prenatal echocardiographic assessment of fetal cardiac function has become increasingly important. Fetal two-dimensional speckle-tracking echocardiography (2D-STE) allows the determination of global and segmental functional cardiac parameters. Prenatal diagnostics is relying increasingly on artificial intelligence, whose algorithms transform the way clinicians use ultrasound in their daily workflow. The purpose of this study was to demonstrate the feasibility of whether less experienced operators can handle and might benefit from an automated tool of 2D-STE in the clinical routine. **Methods** A total of 136 unselected, normal, singleton, second- and third-trimester fetuses with normofrequent heart rates were examined by targeted ultrasound. 2D-STE was performed separately by beginner and expert semiautomatically using a GE Voluson E10 (FetalHQ®, GE Healthcare, Chicago, IL, USA). Several fetal cardiac parameters were calculated (end-diastolic diameter (ED), sphericity index (SI), global longitudinal strain (EndoGLS), fractional shortening (FS)) and assigned to gestational age (GA). Bland-Altman plots were used to test agreement between both operators. **Results** The mean maternal age was 33 years, and the mean maternal body mass index prior to pregnancy was 24.78 kg/m ^{2}. The GA ranged from 16.4 to 32.0 weeks (average 22.9 weeks). Averaged endoGLS value of the beginner was -18.57 % ± 6.59 percentage points (pp) for the right and -19.58 % ± 5.63 pp for the left ventricle, that of the expert -14.33 % ± 4.88 pp and -16.37 % ± 5.42 pp. With increasing GA, right ventricular endoGLS decreased slightly while the left ventricular were almost constant. The statistical analysis for endoGLS showed a Bland-Altman-Bias of -4.24 pp ± 8.06 pp for the right and -3.21 pp ± 7.11 pp for the left ventricle. The Bland-Altman-Bias of the ED in both ventricles in all analyzed segments ranged from -0.49 mm ± 1.54 mm to -0.10 mm ± 1.28 mm, that for FS from -0.33 pp ± 11.82 pp to 3.91 pp ± 15.56 pp and that for SI from -0.38 ± 0.68 to -0.15 ± 0.45. **Conclusions** Between both operators, our data indicated that 2D-STE analysis showed excellent agreement for cardiac morphometry parameters (ED and SI), and good agreement for cardiac function parameters (EndoGLS and FS). Due to its complexity, the application of fetal 2D-STE remains the domain of scientific-academic perinatal ultrasound and should be placed preferably in the hands of skilled operators. At present, from our perspective, an implementation into clinical practice 'on-the-fly' cannot be recommended.

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Methods

A total of 136 unselected, normal, singleton, second- and third-trimester fetuses with normofrequent heart rates were examined by targeted ultrasound. 2D-STE was performed separately by beginner and expert semiautomatically using a GE Voluson E10 (FetalHQ®, GE Healthcare, Chicago, IL, USA). Several fetal cardiac parameters were calculated (end-diastolic diameter (ED), sphericity index (SI), global longitudinal strain (EndoGLS), fractional shortening (FS)) and assigned to gestational age (GA). Bland-Altman plots were used to test agreement between both operators.

Results

The mean maternal age was 33 years, and the mean maternal body mass index prior to pregnancy was 24.78 kg/m^2. The GA ranged from 16.4 to 32.0 weeks (average 22.9 weeks). Averaged endoGLS value of the beginner was -18.57 % ± 6.59 percentage points (pp) for the right and -19.58 % ± 5.63 pp for the left ventricle, that of the expert -14.33 % ± 4.88 pp and -16.37 % ± 5.42 pp. With increasing GA, right ventricular endoGLS decreased slightly while the left ventricular were almost constant. The statistical analysis for endoGLS showed a Bland-Altman-Bias of -4.24 pp ± 8.06 pp for the right and -3.21 pp ± 7.11 pp for the left ventricle. The Bland-Altman-Bias of the ED in both ventricles in all analyzed segments ranged from -0.49 mm ± 1.54 mm to -0.10 mm ± 1.28 mm, that for FS from -0.33 pp ± 11.82 pp to 3.91 pp ± 15.56 pp and that for SI from -0.38 ± 0.68 to -0.15 ± 0.45.

Conclusions

Between both operators, our data indicated that 2D-STE analysis showed excellent agreement for cardiac morphometry parameters (ED and SI), and good agreement for cardiac function parameters (EndoGLS and FS). Due to its complexity, the application of fetal 2D-STE remains the domain of scientific-academic perinatal ultrasound and should be placed preferably in the hands of skilled operators. At present, from our perspective, an implementation into clinical practice 'on-the-fly' cannot be recommended.

Keywords

Cardiac function; speckle-tracking; fetal echocardiography; fetalHQ®; automation; artificial intelligence.

1. Introduction

The knowledge of fetal cardiac function assessment as well as fetal echocardiography itself has advanced dramatically in recent decades [1–5]. With its different modalities, fetal echocardiography has become indispensable for cardiac function assessment [3,6]. With the implementation of fetal echocardiography in clinical routine, two foci arose: the detection of structural congenital cardiac defects (CHD) and subsequently the assessment of fetal cardiac morphometry and function [2,7–10]. Fetal echocardiography is crucial for indirect evaluation of fetal ventricular size and functional parameters since the fetal heart cannot be measured directly *in utero* [11]. A functional cardiac assessment provides early detection of subclinical cardiac dysfunction and detects intrauterine functional cardiac changes and might help to improve and predict perinatal outcomes, including prediction of subsequent cardiovascular risk based on fetal programming [8,12,13]. To record complex fetal myocardial function with its morphometry, encompassing longitudinal, radial, and circumferential deformation (strain), two-dimensional (2D) speckle-tracking echocardiography (STE) provides unique information of cardiac function using myocardial deformation imaging by tracking the endocardial border [2,10,14–16]. Thus, STE allows both, the evaluation and quantification of global and regional, more precisely, segmental biventricular morphometry and function [2,5,6,16–18]. Its variety of quantifiable parameters for comprehensive analysis enables the simultaneous measurements of ventricular as well as atrial size, shape and contractility within a few minutes [14,16,18–24].

The end-diastolic diameter (ED) or the sphericity index (SI) characterizes parameters for fetal cardiac morphometry (ventricular size and shape), and endocardial global longitudinal strain (EndoGLS) or transverse fractional shortening (FS) for fetal cardiac function (ventricular contractility) [2].

Measurement of the ED (syn. 24-segment transverse widths/segment length) of all 24 segments allows determination of the width and change in size of the ventricles and objective assessment of right-to-left disproportion, which is often associated with cardiovascular malformations [21,23].

The SI (syn. 24-segment SI) is calculated by the ratio between the end-diastolic mid-basal apical length divided by each of 24 transverse lengths (SI = end-diastolic length/end-diastolic transverse length), enables assessment of the ventricular shape and is useful to detect abnormal cardiac function resulting from remodeling of the ventricles. [21,22].

The endoGLS, a commonly used deformation parameter [10,14,17], is calculated as the difference in the length of the endocardium from the base of the lateral wall across the apex to the base of the septal wall at end-diastole and end-systole (endoGLS = [(end-systolic endocardial length – end-diastolic endocardial length)/end-diastolic endocardial length] x 100) [19]. In the small fetal heart, measurement of longitudinal global strain appears to be the most accurate and sensitive parameter to visualize pathologies [25], even though others state that the diagnostic and prognostic value of fetal endoGLS has remained uncertain [10]. Because global strain parameters, such as the endoGLS, are less sensitive to local noise and their measurement is more practical, it is considered to be more robust compared to the segmental ones [25,26]. There is still limited data available on the normal ranges of endoGLS during pregnancy [2]. A significant correlation between the endoGLS and the gestational age (GA) is controversially debated in the current literature. Both, an increase and a decrease in endoGLS as well as constant values have been reported previously with advancing GA [2,3,10,14,19,25,27–29]. These conflicting data regarding normal reference ranges and changes of endoGLS complicate the interpretation of current results [14]. Both, abnormal increase and decrease of endoGLS values may indicate cardiac dysfunction, depending on the pathophysiology [12].

The FS (syn. 24-segment transverse FS) is calculated as the difference in the transverse length of each of the 24 segments at end-diastole and end-systole (FS = [(end-diastolic length – end-systolic length)/end-diastolic length] x 100) provides a comprehensive method for assessing ventricular contractility [19–21].

2D-STE has become widely used to assess fetal cardiac function to detect cardiac dysfunction in numerous pathological intrauterine conditions by estimating early fetal cardiac adaptive changes in several pregnancy related complications, including CHD like coarctation of the aorta, aortic or pulmonal stenosis or hypoplastic left ventricle [19–23,30–34], fetal growth restriction (FGR) [17,35], gestational diabetes [36–39], twin-to-twin transfusion syndrome (TTTS) [40,41], pre-eclampsia [42], intrahepatic cholestasis of pregnancy (ICP) [43], fetal non-compaction cardiomyopathy (NCCM) [44,45] or autoimmune diseases [13].

Ultrasound examination is highly examiner-dependent – especially in complex cardiac anatomy – and acquisition and quantification of fetal cardiac functional parameters with accurate prenatal diagnosis by fetal echocardiography depends on the skill and experience of the operator [25,46,47]. The applicability of speckle-tracking is limited when imaging conditions are suboptimal [40]. Therefore, extensive training and education of future experts is of enormous significance [48–51]. Applications based on artificial intelligence (AI), on whose algorithms prenatal diagnostics will rely on increasingly, are transforming the way clinicians use ultrasound [50,52–65].

Recently, we demonstrated the benefit of an automated tool for less experienced operators to assess another cardiac functional parameter, the right ventricular modified myocardial performance index (RV-Mod-MPI) in normal pregnancies [47].

The purpose of this study was to demonstrate the feasibility of whether less experienced operators can handle and might benefit from an automated tool of 2D-STE for offline analysis of diverse parameters for cardiac function in the clinical routine.

2. Materials and methods

2.1. Subjects

In this prospective study, a total of 136 unselected, normal singleton second and third trimester fetuses with normofrequent heart rate were examined during targeted ultrasound survey. All women were routinely investigated by application of Fetal Heart Quantification (fetalHQ®) between August 2021 and January 2024. The used cine-loop sequences were acquired and subsequently analyzed offline by a beginner (J.L.S.) and an expert operator (J.W.) based on consecutively, but independently recorded ultrasound images, and had to fulfill predefined in- and exclusion criteria. Fetuses with structural abnormal hearts and heart rate or clips with insufficient image clarity were excluded. The expert (J.W.) selected both the cine-loop clips recorded by the beginner (J.L.S.), as well as his own and confirmed their applicability for further analysis. It was ensured that the interventricular septum (IVS) had the same orientation between both operators. However, both performed the analysis blinded to each other. Informed consent was obtained from all participants. The measured endoGLS values were matched with those reported in the literature.

2.2. Acquisition of 2D B-mode video clips of the fetal cardiac four-chamber view

As a pre-requisite for 2D-STE analysis, recording of appropriate video clips using a General Electric (GE) Voluson E10 ultrasound device equipped with a trans-abdominal C2-9-D convex probe (2-9 MHz) as well as the software tool fetalHQ(r) (GE Healthcare, Chicago, IL, USA) was performed. The following predefined ultrasound settings were applied: The fetal heart occupied almost 75 % of the screen, corresponding to an appropriate image magnification. The recording of the 2D B-mode cine-loop of the four-chamber view (4-CV) was performed for at least 3 to 5 complete cardiac cycles (approx. 3 seconds (s)), with the IVS optimally oriented as horizontally (apex perpendicular, 90deg) or obliquely (apex oblique up, 45deg) as possible, to visualize the total thickness of the right and left lateral walls of the ventricles as well as the IVS. Care was taken to ensure high contrast between the blood-filled ventricle and the endocardial margin. The frame rate was as high as possible, usually higher than 60 frames/s (Hertz (Hz)). Cine-loops with impairing movement artifacts or insufficient macroscopic identification of endocardial border were excluded, but, to reflect clinical routine, those with suboptimal orientation of the IVS (apex up/down; apex oblique down) were not.

2.3. Application of 2D-Speckle-Tracking-Echocardiography (fetalHQ(r))

The post-processing speckle-tracking, a semiautomated state-of-the-art technique, uses conventional grayscale B-mode frame-by-frame-analysis. As already described elsewhere, this pattern-recognizing method tracks the movement of the speckles representing the movements of the endocardium. They are generated by the interaction of the ultrasound with the endocardial border and show a unique spatial pattern for each region of the endomyocardial interface. Endomyocardial speckles follow tissue motion in all dimensions and their image-processing algorithm-based detection allows the quantitative analysis of velocities and deformations (strain, strain rate) of the myocardium during the cardiac cycle [14].

After measurement of global dimensions at end-diastole (ED) (Figure 1a, Video-Clip S1), for 2D-STE analysis, the raw cine-loop clips of the 4-CVs were loaded into the semiautomated border recognition program fetalHQ(r). Anatomic M-mode (AMM) was used to place a line across the lateral right ventricle wall at the level of tricuspid annulus perpendicularly to the area of interest to define a single cardiac cycle by identifying end-systole (ES) and ED (Figure 1b). The clearest cardiac cycle with best endocardial visualization was selected by determining the first ED and the subsequent ED by marking the nadir on the AMM signal, and finally, the ES (first frame before opening the atrioventricular valve) by marking the peak on the AMM signal (Figure 1c). Once the most optimized cardiac cycle is selected, the systolic endocardial border of each ventricle was automatically tracked algorithm-based by the software in the previously defined end-systole frame along this cardiac cycle by manual identification of three landmarks (three-point-analysis): the septal and the lateral atrioventricular valve annulus as well as the apex, where the consideration of the moderator band required special attention. For the option of more in-depth analyses of the base (1-8), the middle (9-16) and the apex (17-24), both ventricles were divided into 24 segments automatically (cardiac mapping). It was ensured that the course of the generated line of the endocardial border from the right and left ventricles could be tracked from the beginning at the insertion of the atrioventricular valve either on the lateral or septal wall passing the apex and ending at the valve insertion on the opposite wall (Figure 1d and e). If fine tuning was necessary to ensure that the endocardium was adequately traced, end-systolic and -diastolic endocardial tracking were adjusted manually by each operator independently.

Finally, automatically calculated global and segmental parameters for fetal cardiac morphometry and function depicted graphically with superimposed AMM were obtained (Figure 1f). For a better evaluation of the quite complex tool fetalHQ(r), the following parameters were selected and compared for both ventricles: For fetal cardiac morphometry (ventricular size and shape) ED and SI, for fetal cardiac function (ventricular contractility) endoGLS and FS. For simplicity, segments 1, 9, and 17 were selected for the three sections with their 24 segments (base, middle, apex).

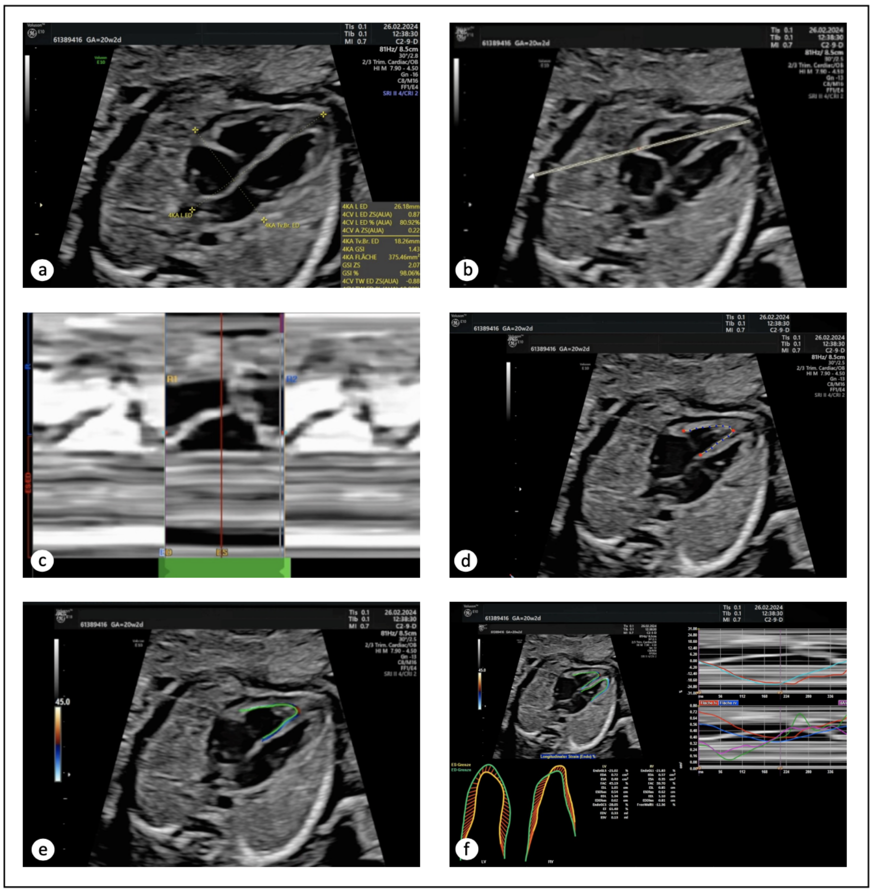

Figure 1: 2D-Speckle-Tracking (2D-STE) analysis using Fetal Heart Quantification (fetalHQ®). a: Determination of the global size and shape of the fetal heart at end-diastole by measurement of two cardiac diameters in the longest dimension; b, c: Identification and selection of an optimal fetal cardiac cycle using anatomical M-mode (AMM); d, e: Manual tracing along the systolic endocardial border in a three-point-analysis (septal and lateral annulus, apex) exemplified for the right ventricle and automatic delineation of the endocardium; f: Landing-page with parameters of fetal cardiac function. EndoGLS = Endocardial longitudinal strain.

2.4. Statistics

All the semiautomatically derived global and segmental parameters were assigned to GA descriptively. The data were compared between the beginner and expert using a Bland-Altman plot (average between the endoGLS, ED, FS or SI of the beginner and expert against the difference between these two) to test the agreement between both operators. GraphPad Prism 10 for Mac (version 10.1.1, GraphPad Software Inc., La Jolla, CA, USA) and Microsoft 365 Excel for Mac (Version 16.8.1, Microsoft Corp., Redmond, WA, USA) were used.

3. Results

The mean maternal age was 33 years (ranging from 20 to 48 years), and the mean maternal body mass index (BMI) prior to pregnancy was 24.78 kg/m2 (range of 17.11 to 36.72 kg/m^2). The GA ranged from 16.4 to 32.0 weeks (average 23.0 weeks) (Table 1).

Characteristics	**Mean (range)**
Maternal age, years	33.19 (20-48)
Nulliparous, %	44.85
Primiparity, %	31.62
BMI prior to pregnancy, kg/m^2	24.78 (17.11-36.72)
Gestational age at targeted ultrasound, weeks of gestation	22.98 (16+3-32+0)
Fetal cephalic presentation, %	58.82

Table 1: Clinical characteristics of the study population (n = 136).

In the 2D-clips of both operators, the IVS was located with ‘apex oblique up’ in 61.76 % (beginner) and in 64.71 % (expert). The mean fetal heart rate was 148 beats per minute (bpm). On average, a frame rate of 76 Hz (beginner) and 73 Hz (expert) in the study collective was achieved. In 43% (beginner) and 7% (expert) of the 2D-clips, the 80 Hz frame rate threshold was exceeded (Table 2).

Characteristics
Orientation of the interventricular septum – beginner, % Apex Up Apex Oblique Up Apex Perpendicular Apex Oblique Do
Orientation of the interventricular septum – expert, % Apex Up Apex Oblique Up Apex Perpendicular Apex Oblique Down
Fetal heart rate – beginner and expert, bpm
Frame rate – beginner, Hz
Frame rate – expert, Hz

Table 2: Technical characteristics of the 2D-clips (n = 136). Bpm = beats per minute; Hz = Hertz.

Averaged endoGLS value of the beginner was -18.57 % ± 6.59 percentage points (pp) for the right and -19.58 % ± 5.63 pp for the left ventricle, that of the expert -14.33 % ± 4.88 pp and -16.37 % ± 5.42 pp (Table 3).

Fetal cardiac parameter	**Ventricle**	**Segment**	**Beginner (mean ± SD)**	**Expert (mean ± SD)**
EndoGLS, %	**RV**	**-**	-18.57 ± 6.59	-14.33 ± 4.88
	LV	**-**	-19.58 ± 5.63	-16.37 ± 5.42
ED, mm	**RV**	**1**	8.89 ± 1.81	9.38 ± 1.85
		9	8.09 ± 1.65	8.42 ± 1.85
		17	5.77 ± 1.34	5.87 ± 1.40
	LV	**1**	8.47 ± 1.96	8.91 ± 1.97
		9	8.20 ± 1.92	8.59 ± 1.81
		17	6.76 ± 1.59	7.09 ± 1.51
FS, %	**RV**	**1**	16.76 ± 10.64	14.45 ± 7.67

Fetal cardiac parameter	Ventricle	Segment	Beginner (mean ± SD)	Expert (mean ± SD)
		9	18.22 ± 9.19	14.95 ± 7.98
		17	15.95 ± 11.82	12.04 ± 12.22
	LV	**1**	11.72 ± 10.73	8.75 ± 10.62
		9	20.73 ± 10.30	21.06 ± 7.62
		17	31.58 ± 12.22	28.49 ± 10.85
SI	**RV**	**1**	1.45 ± 0.30	1.61 ± 0.24
		9	1.59 ± 0.33	1.81 ± 0.30
		17	2.25 ± 0.49	2.63 ± 0.57
	LV	**1**	1.75 ± 0.39	1.89 ± 0.30
		9	1.81 ± 0.43	1.96 ± 0.31
		17	2.19 ± 0.50	2.40 ± 0.45

Table 3: Mean values of both operators. RV = Right ventricle; LV = Left ventricle.

With increasing GA, right ventricular endoGLS decreased slightly while the left ventricular were almost constant (Figure 2).

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Figure 2: Endocardial global longitudinal strain (EndoGLS) versus gestational age (GA): a: RV-EndoGLS; b: LV-EndoGLS. X-axis: GA in weeks. Y-axis: EndoGLS values of beginner (dot) and expert (square) in %. Continuous and dotted lines represent linear regression. FetalHQ® was performed mainly as part of second trimester screening, resulting in a clustering of measurement points in this area. RV = Right ventricle; LV = Left ventricle.

Further average values of both operators for the segmental parameters ED, FS and SI can be found in table 3. Their progression with increasing GA is depicted in Figure S1, S2 and S3 in the supplement. Between beginner and expert, the measured global and segmental parameters indicated a similar distribution (Figure 3 and Figure S4, S5 and S6 in the supplement).

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Figure 3: Distribution of the measured RV-and LV-endocardial global longitudinal strain (EndoGLS) values of both operators: a: RV-EndoGLS; b: LV-EndoGLS. RV = Right ventricle; LV = Left ventricle.

The statistical analysis for endoGLS showed a Bland-Altman-Bias of -4.24 pp (standard deviation (SD) of bias: 8.06 pp; 95% confidence interval (CI) from -1.50 % to -6.97 %) and 95% Limits of Agreement (LoA) from -20.04 % (LoA-, 95% CI from -15.31 % to -24.78 %) to 11.57 % (LoA+, 95% CI from 16.30 % to 6.83 %) for the right and -3.21 pp (SD of bias: 7.11 pp; 95% CI from -0.80 % to -5.62 %) and 95% LoAs from -17.14 % (LoA-, 95% CI from -12.96 % to -21.31 %) to 10.71 % (LoA+, 95% CI from 14.89 % to 6.54 %) for the left ventricle (Table 4, Figure 4).

Fetal cardiac parameter	Ventricle	Segment	Bias (± SD)	95% CI of bias (from to)	95%-LoA$^-$	95%-CI of LoA$^-$ (from to)	95%-LoA$^+$	95%-C LoA$^+$ (from
EndoGLS, %	**RV**	**-**	-4.24 ± 8.06	-1.50 – -6.97	-20.04	-15.31 – -24.78	11.57	16.30 – 6.83
	LV	**-**	-3.21 ± 7.11	-0.80 – -5.62	-17.14	-12.96 – -21.31	10.71	14.89 – 6.54
ED, mm	**RV**	**1**	-0.49 ± 1.54	0.03 – -1.01	-3.50	-2.60 – -4.41	2.52	3.43 – 1.62
		9	-0.32 ± 1.56	0.21 – -0.85	-3.37	-2.46 – -4.29	2.73	3.64 – 1.82
		17	-0.10 ± 1.28	0.34 – -0.53	-2.61	-1.86 – -3.36	2.41	3.16 – 1.66
	LV	**1**	-0.44 ± 1.74	0.15 – -1.03	-3.854	-2.83 – -4.88	2.976	4.00 – 1.95
		9	-0.39 ± 1.71	0.19 – -0.97	-3.73	-2.73 – -4.73	2.95	3.96 – 1.95
		17	-0.33 ± 1.44	0.16 – -0,82	-3.16	-2.32 – -4.01	2.50	3.35 – 1.65
FS, %	**RV**	**1**	2.31 ± 12.63	6.59 – -1.98	-22.44	-15.03 – -29.87	27.06	34.48 – 19.64
		9	3.27 ± 10.57	6.86 – -0.31	-17.45	-11.24 – -23.66	24.00	30.20 – 17.78
		17	3.91 ± 15.56	9.19 – -1.37	-26.59	-17.45 – -35.73	34.40	43.55 – 25.26
	LV	**1**	2.98 ± 14.35	7.85 – -1.89	-25.15	-16.72 – -33.58	31.11	39.54 – 22.68
		9	-0.33 ± 11.82	3.68 – -4.34	-23.49	-16.55 – -30.44	22.83	29.78 – 15.90
		17	3.09 ± 13.95	7.82 – -1.65	-24.26	-16.06 – -32.45	30.43	38.62 – 22.23
SI	**RV**	**1**	-0.17 ± 0.36	-0.04 – -0.29	-0.87	-0.66 – -1.08	0.54	0.75 – 0.33
		9	-0.22 ± 0.44	-0.07 – -0.37	-1.07	-0.82 – -1.33	0.63	0.89 – 0.38
		17	-0.38 ± 0.68	-0.15 – -0.61	-1.71	-1.31 – -2.11	0.95	1.34 – 0.55
	LV	**1**	-0.15 ± 0.45	0.01 – -0.30	-1.03	-0.77 – -1.30	0.74	1.01 – 0.47
		9	-0.15 ± 0.49	0.02 – -0.32	-1.11	-0.82 – -1.40	0.81	1.10 – 0.52
		17	-0.20 ± 0.63	0.01 – -0.41	-1.43	-1.07 – -1.80	1.03	1.40 – 0.66

Table 4: Agreement between both operators. RV = Right ventricle; LV = Left ventricle.

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Figure 4: Bland-Altman plots of agreement between measurements of beginner and expert for endocardial global longitudinal strain (EndoGLS): a: RV-EndoGLS; b: LV-EndoGLS. X-axis: Averages of endoGLS values of beginner and expert in %. Y-axis: Differences between the measured values of beginner and expert in percentage points (pp). Dotted line represents 95 % limits of agreement (LoA) and absolute agreement (y=0) of measurements and continuous line represents Bland-Altman bias. Shaded areas represent 95 % confidence interval (CI) limits for bias and LoA. RV = Right ventricle; LV = Left ventricle.

The Bland-Altman-Bias of the ED in both ventricles over all analyzed segments ranged from -0.49 mm ± 1.54 mm to -0.10 mm ± 1.28 mm, that for FS from -0.33 pp ± 11.82 pp to 3.91 pp ± 15.56 pp and that for SI from -0.38 ± 0.68 to -0.15 ± 0.45 (Table 4, Figure S7, S8 and S9 in the supplement).

4. Discussion

Beyond a scientific context, how does speckle-tracking analysis using fetalHQ® perform in routine clinical practice and could less experienced operators benefit from this state-of-the-art technique? The present study aimed to scrutinize the applicability of 2D-STE based on the expertise of two operators.

Quantification of fetal myocardial function is challenging, and several different techniques have been used [6,14,25,66]. Already in 2012, Crispi et al. stated that in expert hands and with adequate ultrasound equipment, accurate assessment of cardiac function is feasible in most fetuses [4,8]. With the continuous development of AI algorithms and their implementation in platforms of different ultrasound devices, two softwares – MPI+™ (Samsung Healthcare, Gangwon-do, South Korea) and fetalHQ® (GE Healthcare, Chicago, IL, USA) – have recently been established to examine different cardiac functional parameters of the fetus. So far, only the learning curve for the acquisition of the MPI manually [67] and the benefits of its semiautomatically measurement in clinical routine for less experienced operators have been demonstrated [47]. The additional value of the 2D-STE for less experienced sonographers has yet to be demonstrated, although the significance in a scientific setting is undisputed.

FetalHQ® has shown excellent reproducibility for the analysis of morphometric as well as functional cardiac parameters [2,7,14,16]. Based on our data, we were able to demonstrate good to excellent agreement between both operators for the applicability of 2D-STE for comprehensive analysis of global and segmental cardiac deformation. Although, current studies have recently questioned the initially excellent reproducibility of segmental parameters in particular [2,5,68,69].

Despite all the advantages that 2D-STE can offer in combination with post-processing analysis using fetalHQ®, the technique mainly depends on the skill and experience of the operator and the quality of acquisition of an optimal clip of the 4-CV [14,25,70]. An experienced operator of prenatal ultrasound will certainly undergo a short learning curve to acquire and analyze short image-optimized cine-loop sequences of the fetal cardiac 4-CV by 2D-STE [69,71]. For less experienced operators with initially lack of adaptive skills in visualizing an optimal 4-CV of the fetal heart, a marked learning curve can be assumed. Germanakis et al. summarized that, although speckle tracking technique is algorithm-guided, offline image analysis is not user-independent. The operator must place or adjust the endocardial tracking lines. Therefore, a learning curve is essential prior successful implementation in clinical routine [5,10,15,25,71]. To take these aspects into account and to achieve the same level of standardization as in adult cardiology, DeVore et al. have provided a practical step-by-step approach [16].

The classification of the cardial functional parameters in the pathophysiological context and their subsequent interpretation is highly complex. Due to differences in ultrasound equipment, measurement techniques with non-standardized pre-settings, non-systematic image settings and processing, vendor-specific analysis software with different algorithms tracking speckle patterns and myocardial deformation as well as maternal and fetal characteristics of the study population [2,5,12,14], a wide variability in the quoted endoGLS reference values during pregnancy results to date. Since there is neither a mandatory standardization of the process nor of the semiautomatic algorithms, and there are many pitfalls to deal with, the cardiac function parameters described in the literature vary considerably [2,5,7,8,12,14,25]. It should also be noted that any normal reference ranges of myocardial deformation may need to be adjusted to the corresponding GA [14]. Patey et al. reported on intervendor discrepancies with significant clinical and research consequences. They demonstrated that fetal 2D-STE assessments are reliable when performed on the same ultrasound platform, while ultrasound machines and software from different vendors produce significantly different fetal 2D-STE parameter estimates. This should be considered when interpreting and comparing research data [72]. The review by Kühle and co-workers revealed that the mean value of all cited studies – excluding those with positive values – considered for the right ventricular GLS is reported as -19.36 % ± 4.55 pp, that of the left as -19.21 % ± 3.88 pp. The lowest cited value for the right ventricular GLS was -35.88 %, the highest -12.80 % and the lowest left ventricular GLS -26.01 %, the highest -12.30 % [25]. The mean endoGLS values of both operators in this paper are consistent with those referenced in the literature. It is widely recognized that fetal circulation is right-heart-dominant with higher myocardial shortening during contraction in the right ventricle [11,25,73,74]. The more negative the endoGLS values, the better the contractility of both ventricles [10,14]. It would therefore be expected that longitudinal strain values in the right ventricle are between 1.0 and 1.5 times higher (i.e. more negative) compared to the left ventricle due to the difference in myofiber orientation [40,75], although contradictory measurements can be found in literature concerning this as well [10]. As many other studies, we were unable to confirm this hypothesis based on our data (Table 3, Figure 2 and 3) [25]. Echocardiographic evaluation of ventricular function is challenging, especially assessment of the right ventricle function due to its complex anatomy [76]. On the one hand, anatomical structures like the moderator band can complicate the correct placement of the apical caliper for the operator, on the other hand prominent trabeculation can impair the automatic delineation of the endocardial border during a cardiac cycle by the software [5,25,75]. Such inaccuracies in the acquisition of right ventricular deformation parameters with suboptimal contrast between the endocardium and the respective ventricular chamber without precise wall tracking might result in underestimated endoGLS values [10,25]. Furthermore, 2D-STE is only based on 2D 4-CV, which neglects spatial aspects of cardiac anatomy of the right ventricle. This might apply to our data, with lower mean endoGLS value of the left compared to the right ventricle (Table 3, Figure 2 and 3). In addition, the agreement of the right ventricular endoGLS measurements between the two operators in our study is lower compared to left ventricular (Table 4, Figure 4). This assumption of lower agreement for right ventricular parameters was also reported by Huntley et al. [5]. Altogether, all measured functional parameters in our study – global as well as segmental – showed good to excellent agreement between both operators (Table 4, Figure 4 and S7 to S9). The lowest agreement, but still considered as good, was found for the FS. These results are in accordance with recent publications questioning the reproducibility of FS, which was previously reported as excellent [2,5,68]. It was also noticeable in our study that the absolute values of the FS of the individual segments frequently deviated from the percentages defined in the software fetalHQ®. The focus of this study was not the determination of further reference values or the verification of reproducibility of fetalHQ®, but rather the proof of agreement between two operators of different expertise. Nevertheless, this aspect should be mentioned. 2D-STE can be used throughout pregnancy, even as part of first trimester screening [25,77]. However, in clinical routine, we emphasize its best application mid-gestational and advanced GA, as other authors have also elaborated [5,10,14,25,28,29]. Our endoGLS values of both ventricles assigned to gestational age are consistent with the contradictory data in the literature, with slight decrease of right ventricular and almost constant left ventricular endoGLS values with increasing GA (Figure 2). Ohira et al. recently reported on similar findings with their underlying pathophysiological mechanisms [28].

In fact, 2D-STE should have better intra- and interobserver variability than other techniques used to evaluate cardiac function [16]. Apart from routinely acquired 2D B-mode images of the 4-CV, no further imaging is required. In contrast to Doppler-based methods, 2D-STE is supposed to be angle-independent due to the simple acquisition of the 2D image, regardless of the orientation of the heart to the ultrasound beam, and could therefore be performed in any fetal position [15,16,27]. It is controversially discussed that speckle tracking is less angle-dependent or even angle-independent [2,5,10,12,14,16,17,36,40,78]. Most likely – and we agree with this opinion – 2D-STE can be considered as less angle-dependent but cannot be performed in every fetal position with limited clip acquisition of the 4-CV. At least the position of the IVS should be considered when a cine-loop of a 4-CV is recorded. In clinical routine, it is almost impossible to record every fetal heart with the IVS in a perpendicular position, as recommended by deVore et al. [16]. In our study, the most common apex orientation for both beginner and expert was 'apex oblique up' (Table 2). Furthermore, due to the combination of small size of the fetal heart with high heart rate, an adequate frame rate to achieve a high temporal and spatial resolution with tracking of the speckles is intensively discussed [2,5,6,8,9,14,16,25]. 2D-STE requires a high resolution 4-CV, suitable for post-processing analysis, with high image acquisition frame rate, depending on fetal heart rate [2,6,15,16,25,78]. Specialized software with an automated sensitive and accurate border recognition can contribute to simplify and standardize the procedure of speckle tracking [6,11]. However, the quality of subsequent speckle tracking analysis is affected by the proper visualization of the 4-CV within the cine-loop with clear delineation of the endocardium [5,24,25]. Precise image acquisition and quality of the 4-CV can be impaired by maternal BMI, anterior placenta, oligohydramnios, fetal anatomy and position, resulting artifacts caused by maternal as well as fetal movements and, not least, from skills of the operator. Since the number of ultrasound frames per second is assumed to have a great impact on the reliability of 2D-STE, DeVore et al. recommend an optimal frame rate of >80 Hz. But there is currently no consensus about the optimal frame rate for strain imaging with recommendations for significantly higher frame rates [25,28,79,80]. On average, we achieved a frame rate of 76 Hz (beginner) and 73 Hz (expert) in our study collective, which represents the clinical routine (Table 2). Gireadă et al. exceeded the 80 Hz frame rate threshold in only 9%, we in 43% (beginner) and 7% (expert) [36]. When interpreting the results of a speckle tracking analysis and assessing the agreement of measurements between operators, angel of insonation (apex orientation) and frame rate must be kept in mind.

In our opinion, there are three pitfalls with significant impact on the accuracy, reliability and validity of the method as well as the agreement between the operators that must be considered when performing 2D-STE: Firstly, the artifact-free image acquisition of a clip of the 4-CV, secondly, the orientation on the heart with recognition of the left and right side, as well as subsequent identification of an optimal cardiac cycle, thirdly, the manual placement of the three calipers with any required adjustment of the endocardial tracking lines. Considering these aspects, a short learning curve is also evident for less experienced operators. We emphasize that 2D-STE cannot be applied in all patients. In contrast to RV-Mod-MPI, it requires a good pre-selection for success. Compared to other methods for the determination of fetal cardiac function, such as the RV-Mod-MPI, the time factor has a significant negative impact on the 2D-STE analysis. The evaluation of the complex measurements is more time-consuming and requires further expertise. The longer the cine-loop, the longer the import into the software for further analysis. Therefore, 2D-STE analysis is less suitable for performing 'on-the-fly' in the busy, tightly scheduled clinical routine, especially for less experienced operators. Despite today's semiautomatic 2D-STE measurement using fetalHQ® and after more than ten years since Van Mieghem et al. concluded that speckle tracking can be performed by a sonographer with limited experience in fetal cardiology on any prenatal ultrasound exam, we still doubt this statement even in 2023 [40]. We agree with the opinion of Germanakis et al. who underline the importance of understanding the basic principles of strain and the resulting limitations of 2D-STE before adopting it into routine clinical practice [15].

An approach to optimize the performance of the 2D-STE method more efficient with shorter time for acquisition was recently published. The quiver technique enables the operator to identify the endocardial borders more precisely and efficiently. It facilitates the identification of the septal and lateral atrioventricular valve annulus by cine-looping two frames before and after the selected end-systolic and -diastolic frame [24]. In our opinion, it will be of great importance in the future to eliminate human manual adjustment for improving reproducibility and increasing efficiency in daily clinical routine by automatically identifying the most optimal cardiac cycle including the accurate selection of endocardial borders by AI algorithms. This was already demanded by Huntley et al. [5].

Although speckles move in three dimensions, most methods of speckle tracking are based on post-processing analysis of only one acquired plane of a 2D-clip of the fetal heart [9,14]. Speckles beyond the insonated plane will not be analyzed [6]. Cardiac mechanics is complex due to special geometry with myocardial three-directional motion including longitudinal, radial, and circumferential contraction [4,8,25,73]. The helical structure of the ventricular myocardium with its three-dimensional (3D) deformation requires to detect speckles in all dimensions [81]. In addition, 2D-STE excludes the right ventricular outflow tract [11]. Theoretically, holistic, spatial concepts might offer an important contribution in measuring more realistic volumetric parameters. It therefore seems natural to combine STE technique with spatial methods such as 3D- or four-dimensional (4D)-spatio temporal image correlation (STIC) for a more precise and realistic measurement and to overcome B-mode imaging limitations of 2D-STE [2,9,70,82].

Once a suitable 2D-clip of the 4-CV was acquired with knowledge of the pitfalls discussed above, there was in many cases nothing to prevent subsequent offline analysis using fetalHQ® and resulted in high agreement between beginner and expert. Nevertheless, some limitations of the present study must be mentioned. Only 136 unselected, normal, singleton, second- and third-trimester fetuses without CHD in healthy women, focusing on the 23th week of gestation on average, were examined. The period in which these clips for 2D-STE analysis were recorded appears to be quite long. The recording of the clips with subsequent 2D-STE analysis was performed by only two operators. However, these two (beginner and expert) were representative as holders of DEGUM level 1 (German Society for Ultrasound in Medicine), the minimum standard for a sonographer, and DEGUM level 3 for gynecology and obstetrics. The former certifies familiarity with the basics of ultrasound diagnostics, the latter characterizes a proven expert far beyond basic knowledge. Representative for the base (1-8), the middle (9-16) and the apex (17-24) of both ventricles, in this study, according to Nogué et al., segments 1, 9 and 17 were selected for comparison of measurements of both operators [2]. It would be possible to select other segments, for example 1, 12 and 24, as in the study of Zhu et al. [11]. Differences in the agreement of both operators in the measurement of segments not examined are feasible, which applies to segmental, but not to global parameters. In this study, we allowed orientations of the IVS that were considered suboptimal for 2D-STE analysis to reflect daily clinical routine. According to our results, this did almost not impair the good to excellent agreement between the two operators.

5. Conclusions

Between both operators, our data indicated that 2D-STE analysis showed excellent agreement for cardiac morphometry parameters (ED (ventricular size) and SI (ventricular shape)), and good agreement for cardiac function parameters (EndoGLS and FS (ventricular contractility)). For less experienced operators to benefit from this state-of-the-art technology, a number of obstacles obviously still need to be overcome. With knowledge of these pitfalls, the 2D-STE analysis method can be learned efficiently and performed with a high level of expertise. However, as long as the performance of a 2D-STE analysis will not be completely standardized and automated, we cannot recommend its use in clinical routine for comprehensive fetal cardiac functional analysis by less experienced operators 'on-the-fly', despite good to excellent agreement of global and segmental deformation parameters between both operators. AI will facilitate the implementation of 2D-STE analysis in daily clinical practice. At present, from our perspective, due to its complexity, the application of fetal 2D-STE remains the domain of scientific-academic ultrasound perinatal diagnostics and should be placed preferably in the hands of skilled operators.

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