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Transition from fetal to neonatal life: Changes in cardiac function assessed by speckle-tracking echocardiography

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ABSTRACT

Objective: Assessment of cardiac function by speckle-tracking (2D-S) echocardiography in the transitional period from fetal to neonatal life in a healthy population.
Methods: Ultrasound assessment of cardiac function of 30 healthy fetuses at the gestational age of 28 weeks, and follow-up after birth using 2-D strain derived novel parameters such as longitudinal strain (S), strain rate (SR), tissue velocities, MPI- and E/E′-index, E/A- and E′/A′-rate of both right (RV) and left ventricles (LV) and interventricular septum (IVS) and comparison to conventionally measured cardiac stroke volume (SV), cardiac output (CO) and ejection fraction (EF).
Results: Ultrasound 2D-S performance and analysis were technically feasible and reproducible in all 30 fetuses and in the neonatal period. In fetuses, tissue velocities and SR measurements were homogenous for all regions of interest in both ventricles, and strain increased from apex to base and was significantly higher in the RV compared to LV. All calculated indices were almost identical for RV and LV.
After birth, strain and strain rate exhibited significantly lower values, and systolic tissue velocities were higher in comparison to fetal values in both chambers and in all regions of interest.
Conclusion: Speckle-tracking echocardiography is a feasible and reproducible technique in analyzing both fetal and newborn cardiac functions. Therefore, it might be useful in clinical routine examinations and give new insights in transitional physiology.
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1. Introduction

The relatively new technique of speckle-tracking echocardiography has been used successfully in the animal model and in humans to evaluate regional and global myocardial function. The technique consists of a frame-to-frame tracking of the ultrasound signal backscatter in the myocardium, measuring the velocity (cm/s) of displacement of the chosen myocardial region of interest, the deformation (strain %) and deformation rate (strain rate 1/s).

Adapting this ultrasound tool to a fetal cohort implied many problems due to fetal position, small cardiac size, high heart rates and mothers' obesity. Nevertheless, a few studies have been performed in fetal cohorts that showed relatively good reproducibility and feasibility [1–7]. This is mainly due to the fact that investigations could be adjusted at higher frame rates [7] and that angle correction was obsolete—in contrast to tissue Doppler-derived signals, which have shown to be very angle-dependent.

Different equipment and algorithms have been used in the analysis of ultrasound signals mostly to establish normal values in healthy fetal [8,9] and pediatric [10,11] populations at different gestational and postnatal ages. A few studies have been focused on cardiac pathologies and congenital malformations [12,13], some of them concentrating on special fetal conditions, such as intra-amniotic infection [14] and twin-to-twin-transfusion syndrome [15].

To our knowledge, this is the first study that assesses cardiac function in the transitional period from fetal to neonatal life in a healthy and homogenous population using speckle-tracking technique, to compare the results to conventionally performed echocardiography and to discuss them in relation to changes in load in the feto-neonatal transition.

2. Methods

This observational study measured fetal and postnatal myocardial function and performance using conventional echocardiography and the speckle-tracked longitudinal strain, strain rate and tissue velocity in healthy infants. The study protocol was approved by the regional

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ethics committee, and parental informed consent was obtained before each examination.

2.1. Subjects and study protocol

The study group comprised 30 (11 boys) healthy fetuses at the gestational age of 28 + 0 to 28 + 6 (mean 28 + 3) weeks, who were later born at term and examined on average 170 (range 135–207) hours postnatally at Karolinska University Hospital between November 2008 and May 2009. All subjects were singletons, without any malformations and appropriate for gestational age, defined as a birth weight within ±2 standard deviations (SD) from the mean for normal weight according to Swedish sex and gestational age-specific reference data. Recruitment and enrollment of the mothers were performed at a scheduled routine antenatal visit in the second trimester at three primary health care maternity clinics. After having received detailed information, 30 interested mothers contacted us and were included in the study. No further recruitment was necessary as there were no drop outs. Gestational age had been prospectively determined in all pregnancies by routine fetal ultrasound examination at 17–18 postmenstrual weeks, a complete anomaly scan including cardiac anatomy was performed at this date and confirmed the healthy state of all fetuses.

2.2. Ultrasonographic assessments

All recordings were performed by one experienced examiner (U.S.) using the same ultrasound machine (GE Vingmed Vivid 7, General Electric, Horten, Norway, http://www.ge.com/no/) and a phased array matrix sector probe (GE M3S 1.5–4.0 MHz) for fetal, and another phased array sector probe (GE 10-S 4.0–10.5 MHz) for infant examinations. A complete diagnostic echocardiographic assessment was performed in all subjects to rule out malformations and significant patent arterial duct in the newborn infants. For each examination, digital loops containing at least five heart cycles in a B-Mode apical 4-chamber-projection were acquired in high 2D-quality and at frame rates ranging between 147/s and 180/s (mean 163/s) in the fetal, and between 176/s and 200/s (mean 187/s) in the neonatal group. In order to obtain comparable frame rates, apical 2-chamber views including either the right or left ventricle and the corresponding atrium were recorded in some examinations, no harmonic imaging was used.

All recordings were evaluated off-line by an independent examiner (M.M.), using commercially available software (Echo-PAC, GE Healthcare, USA). A semi-automatic system traced the myocardium/endocardium border of each ventricle in separate analyses marking 6 regions of interest (ROI). When necessary, the tracking process was optimized by the examiner visually, as the midpoint of the endocardial tracking line was not necessarily the anatomical apex of the respective ventricle.

We measured at atrio-ventricular annulus, mid-septal and apical level in the free walls of the left (LV) and right ventricle (RV) and the interventricular septum (IVS) in systole and diastole. Three measurements were performed for each parameter and the mean value calculated. Values for the interventricular septum were assessed in the analysis of the left ventricle. However, there were no significant differences when compared to IVS measurements from the right ventricle. In fetal investigations, we used a dummy ECG based on mitral and aortic valve motion in order to define systole and diastole.

The underlying software measured velocity by the derivation of speckle displacement per time unit and Lagrangian strain by the temporal integration of strain-rate, where peak longitudinal strain defines the relation between initial (=L0) and final (=L) maximal length of right and left ventricular free walls: $\varepsilon = L - L0 / L0$.

2.3. Calculation of cardiac indices

The myocardial performance index (MPI) was calculated by measuring the isovolumetric contraction (ICR) and relaxation (IRT) time before and after ejection time (ET) of the left and right chamber.

$$MPI = ICT + IRT/ET.$$

The relation between early diastolic filling velocities (E) measured by the conventional PW-Doppler and the speckle-tracking technique (E′) is represented by the quotient E/E′. The relation between early (E) and late (A) diastolic filling is expressed in the quotient: E/A in the conventional PW-Doppler and E′/A′ in speckle-tracking technique.

Stroke volume and cardiac output were measured with the help of Doppler derived flow velocity integrals according to the formulas:

$$SV = \text{velocity time integral} \times \text{valve area} \quad CO = SV \times \text{heart rate}.$$

In addition to that, conventional planimetry was performed for both chambers using the Simpson formula:

$$EF = (\text{enddiastolic area} - \text{endsystolic area})/\text{enddiastolic area}.$$

3. Statistics

Descriptive statistics were presented as mean and standard deviation for numerical variables, or as percentages for categorical variables. Taking 80% power and 5% significance level, and considering a minimum expected difference of 3%.and standard deviation of 4.0 for the primary outcome variable of mean fetal and neonatal strain, a sample size of 28 individuals was required for the study (www.openepi.com). The Shapiro Wilk's test was performed to test normality. If $p > 0.05$, the data distribution was considered to be normal. In addition, skewness was also examined to determine the normality of the distribution. A skewness value within a +1 to −1 range was considered as normally distributed data. A paired *t*-test was used to test the null hypothesis that there was no difference in the means between the fetal and neonatal values. When there was deviation from normality due to outliers, we performed the paired *t*-test with and without outliers. Statistical analysis was performed using JMP software (JMP 9.0.1 SAS Institute, Inc., Cary, NC, USA). The level of significance was specified at 5% for all tests. Ten randomly chosen recordings were re-analyzed by the same examiner at a later time and again by another investigator (U.S.) in order to calculate the intra- and inter-observer variability of the different techniques.

4. Results

Almost all measurements were normally distributed, but a few variables showed a slightly skewed distribution due to the outlier problem (the highest skewness value was 1.58). However, we did not observe statistically significant differences when the analysis was examined with and without outliers. The intra-observer variability was calculated to be 5.8% for the speckle-tracking technique and 9.8% for the conventional ultrasound, and the inter-observer variability was 6.5% and 10.7%, respectively. The maximum error when changing transducer ranged from 0.1% to 2.0%, according to General Electric, Horten, Norway.

4.1. Fetal myocardial tissue velocities

The mean peak velocity at the bases of the RV and LV as well as of the IVS ranged from 3.28 to 4.83 cm/s for systolic, early diastolic and late diastolic filling, with the chambers moving towards the transducer in systole, and therefore exhibiting positive velocity values, and moving from the transducer, and therefore showing negative measurements in

Table 1
Maximal basal velocities (cm/s) of the right ventricle (RV), left ventricle (LV) and interventricular septum (IVS) in systole (S), early diastole (E) and late diastole (A) in echocardiographic examinations at 28th week of gestation (fetal) and after birth (neo). Positive and negative values indicate the systolic and diastolic movement of the heart in relation to transducer position.

		Mean (SD), fetal	Mean (SD), neo	Δ Mean	95% CI	t	p-Value
RV	S	4.83 (1.86)	6.38 (2.34)	−1.55	−0.47; −2.57	−2.98	0.006
	E	−4.40 (1.93)	−6.62 (1.24)	−2.22	−1.09; −2.88	−4.55	<0.001
	A	−4.53 (2.30)	−5.97 (2.52)	−1.44	−2.7; 0.02	−2.03	0.053
LV	S	4.49 (1.56)	4.44 (1.45)	0.05	−0.82; 0.83	0.00	0.99
	E	−4.70 (1.60)	−5.51 (1.84)	−0.81	−1.66; 0.07	−1.89	0.07
	A	−4.71 (1.49)	−4.22 (1.86)	0.49	−0.57; 1.43	0.87	0.39
IVS	S	4.27 (1.44)	4.00 (1.13)	0.27	−1.00; 0.48	0.74	0.46
	E	−3.28 (0.71)	−5.02 (1.83)	−1.74	−0.67; −2.77	−3.36	0.002
	A	−4.11 (1.73)	−4.82 (1.84)	−0.71	−1.57; 0.15	−1.70	0.10

Δ Mean is indicating the mean difference (fetal value–neonatal value).
Data are mean (SD), 95% confidence interval (95% CI), t- and p-values according to paired *t*-test.

diastole. The obtained velocity values did not differ significantly although there was a trend of decreasing peak velocities from RV to LV and IVS (p-values from 0.37 to 0.78). As expected, late diastolic filling velocities were higher compared to early diastolic filling peak velocities (Table 1).

4.1.1. Fetal strain-rate

In contrast to wall velocity measurements, systolic strain-rates exhibited negative values compared to positive results in early and late diastole. There is a clear trend of higher strain-rates at the base of the heart compared to more apical parts (p-values from <0.001 for late right ventricular diastolic SR to $p = 0.09$ for systolic SR of the IVS comparing basal to medial parts of the heart). In addition, strain-rate values were significantly higher in the right compared to the left ventricle (p-values from 0.01 for late diastolic SR at base to $p = 0.03$ for early diastolic SR at base). The overall strain-rate varied from 3.35 to 5.34 per second (Table 2).

4.1.2. Fetal longitudinal strain

Table 3 shows significantly higher systolic strain values ($p < 0.001$) in the right chamber compared to IVS and LV. In addition, strain was higher in the basal parts of the left and right chambers in comparison to more apical ROI ($p = 0.001$ for RV, $p = 0.02$ for LV and $p = 0.002$ for IVS comparing basal and medial parts of the heart). The mean strain in the RV was −27.3% and −22.2% in the IVS and the lateral wall of the LV.

4.1.3. Fetal cardiac indices

All calculated cardiac indices were homogenous for each measurement and almost identical for the left and right ventricles. As presented in Table 4, the relation between Doppler-derived early diastolic velocity and speckle-tracked-derived early wall velocity (E/E′) was 11.5 in the LV and 11.3 in the RV. The calculated relation between early and late diastolic filling was 0.88 for the RV and 0.91 for the LV in the PW-Doppler, and 1.12 (RV) and 1.06 (LV) by speckle-tracking method.

Table 2
Maximal strain-rate (1/s) of the right ventricle (RV), left ventricle (LV) and interventricular septum (IVS) in systole (S), early diastole (E) and late diastole (A) at the base, midventricular (medial) and apex in echocardiographic examinations at 28th week of gestation (fetal) and after birth (neo). Positive and negative values indicate the systolic and diastolic movement of the heart in relation to transducer position.

			Mean (SD), fetal	Mean (SD), neo	Δ Mean	95% CI	t	p-Value
RV	Basal	S	−5.26 (2.08)	−3.61 (1.59)	1.65	−0.01; 2.57	2.03	0.05
		E	5.34 (2.36)	3.63 (2.07)	1.71	0.34; 2.94	2.59	0.015
		A	4.68 (1.88)	2.95 (1.61)	1.73	0.58; 2.71	3.18	0.003
	Medial	S	−4.68 (1.85)	−2.86 (1.08)	1.82	0.92; 2.67	4.21	<0.001
		E	4.75 (2.24)	3.24 (1.42)	1.51	0.41; 2.67	2.81	0.009
		A	3.77 (1.45)	2.40 (1.24)	1.37	0.58; 2.11	3.63	0.001
	Apical	S	−4.69 (2.05)	−2.45 (0.75)	2.24	1.45; 3.12	5.66	<0.001
		E	4.62 (2.26)	2.90 (1.16)	1.72	0.30; 2.86	2.54	0.01
		A	3.80 (1.56)	1.95 (0.87)	1.85	0.95; 2.35	4.80	<0.001
LV	Basal	S	−4.44 (1.42)	−2.94 (1.05)	1.50	1.00; 2.43	4.90	<0.001
		E	4.01 (1.56)	3.50 (1.25)	0.51	−1.2; 0.14	1.62	0.12
		A	3.62 (1.34)	2.59 (1.48)	1.03	0.35; 2.41	2.74	0.01
	Medial	S	−3.87 (1.05)	−2.37 (1.14)	1.50	1.23; 2.44	6.18	<0.001
		E	3.38 (1.42)	2.90 (1.02)	0.48	−1.08; 0.14	1.59	0.12
		A	3.45 (1.42)	2.13 (0.97)	1.32	0.67; 2.10	3.96	<0.001
	Apical	S	−3.84 (0.70)	−2.47 (0.78)	1.37	1.18; 2.20	6.76	<0.001
		E	3.68 (1.29)	3.06 (0.89)	0.62	0.09; 1.19	2.39	0.02
		A	3.35 (1.17)	2.52 (1.31)	0.83	0.05; 1.49	2.20	0.03
IVS	Basal	S	−4.25 (1.47)	−2.32 (0.77)	1.93	1.43; 2.89	6.03	<0.001
		E	4.00 (1.49)	2.52 (1.34)	1.48	0.89; 2.90	3.86	<0.001
		A	3.81 (1.59)	2.25 (1.03)	1.56	0.89; 2.73	4.04	<0.001
	Medial	S	−3.98 (1.42)	−2.05 (0.79)	1.93	1.72; 3.47	6.09	<0.001
		E	3.53 (1.13)	2.37 (0.90)	1.16	0.85; 2.28	4.48	<0.001
		A	3.61 (1.60)	1.95 (0.77)	1.66	1.06; 2.46	5.16	<0.001
	Apical	S	−4.03 (1.30)	−2.07 (0.65)	1.96	1.72; 3.40	6.25	<0.001
		E	3.99 (1.49)	2.69 (0.97)	1.30	0.62; 2.05	3.83	<0.001
		A	3.67 (1.47)	2.01 (0.96)	1.66	1.10; 2.50	5.31	<0.001

Δ Mean is indicating the mean difference (fetal value–neonatal value).
Data are mean (SD), 95% confidence interval (95% CI), t- and p-values according to paired *t*-test.

Table 3
Maximal and mean systolic longitudinal strain (%) of the right ventricle (RV), left ventricle (LV) and interventricular septum (IVS) at the base, mid-ventricular (medial) and apex in echocardiographic examinations at 28th week of gestation (fetal) and after birth (neo). Negative values indicate the systolic movement of the heart in relation to transducer position.

		Mean (SD), fetal	Mean (SD), neo	Δ Mean	95% CI	t	p-Value
RV	Basal	−29.3 (6.4)	−25.3 (7.3)	4.0	−0.3; 7.8	1.91	0.06
	Medial	−26.5 (4.4)	−22.6 (4.7)	3.9	1.5; 6.4	3.31	0.003
	Apical	−26.0 (4.9)	−21.2 (5.0)	4.8	2.1; 8.1	3.50	0.001
	Mean	−27.3 (4.4)	−23.0 (4.3)	4.3	1.7; 6.8	3.41	0.002
LV	Basal	−23.9 (4.3)	−20.0 (3.8)	3.9	1.5; 6.2	3.33	0.002
	Medial	−21.8 (3.3)	−19.1 (2.6)	2.7	1.4; 4.5	3.81	<0.001
	Apical	−22.1 (3.6)	−19.3 (2.7)	2.8	0.3; 3.9	2.38	0.02
	Mean	−22.2 (2.9)	−19.5 (2.1)	2.7	1.5; 4.4	4.14	<0.001
IVS	Basal	−24.3 (5.4)	−20.6 (3.6)	3.7	0.9; 5.6	2.77	0.01
	Medial	−22.9 (4.6)	−19.6 (3.5)	3.3	0.8; 5.6	2.78	0.009
	Apical	−22.1 (3.6)	−19.3 (2.7)	2.8	−0.4; 4.0	1.61	0.11
	Mean	−22.2 (2.9)	−19.5 (2.1)	2.7	0.6; 5.2	2.60	0.01

Δ Mean is indicating the mean difference (fetal value–neonatal value).
Data are mean (SD), 95% confidence interval (95% CI), t- and p-values according to paired *t*-test.

The MPI, too, was identical for both ventricles (0.26), demonstrating only a very small variation of measurements.

4.1.4. Fetal ejection fraction (EF), stroke volume (SV) and cardiac output (CO)

The EF measured with the Simpson method was similar for both ventricles (65.29% for the RV and 64.66% for the LV). The SV and CO differed significantly between both ventricles, with the RV contributing approximately 58% to the combined cardiac output (443 ml/min vs 321 ml/min, CO-ratio 1.4:1).

4.2. Neonatal myocardial tissue velocities

The peak velocity at the bases of the RV and LV, as well as at the IVS, ranged from 4.00 to 6.62 cm/s for systolic, early diastolic and late diastolic filling. Only systolic and late diastolic velocities in the LV and IVS continued almost unchanged. All other values increased after birth, especially in the RV which exhibited significantly higher velocities compared to LV ($p = 0.002$) and IVS ($p = 0.001$) (Table 1).

4.2.1. Neonatal strain rate

Values for all regions of interest both in systole and diastole decreased considerably (with the exception of early diastolic strain rate in the LV)-representing highly significant differences as compared to fetal life. The trend of higher strain rates at the base of the heart compared to more apical parts remained unchanged even after birth ($p = 0.001$ for systolic strain in RV, LV and IVS comparing basal and medial parts of the heart). Strain rate values continued to be higher in the RV compared to the IVS ($p = 0.001$ for systolic SR) and LV, though not longer exhibiting significant differences (p-values from 0.08 for systolic SR at base to 0.81 for systolic SR at apex) (Table 2).

4.2.2. Neonatal longitudinal strain

After birth, systolic strain values are still higher in RV in comparison to LV ($p < 0.001$) and IVS ($p = 0.004$), and also higher in the basal parts of the heart ($p = 0.01$ for RV, $p = 0.09$ for LV and $p = 0.002$ for IVS comparing basal and medial values). In comparison to fetal measurements, postnatal systolic strain values decreased significantly in all assessed regions and in both ventricles (Table 3).

4.2.3. Neonatal indices

Concerning the LV, MPI and E/E′ remained almost unchanged in the postnatal period. The calculated relation between early and late diastolic filling (E/A) increased from 0.91 to 1.11 and E′/A′ from 1.06 to 1.48 and E/E′ from 11.5 to 11.8.

MPI (0.17, $p < 0.01$) and E/E′ (8.7, $p = 0.07$) were lower in the RV after birth, and E/A increased from 0.88 in fetuses to 1.0, and E′/A′ from 1.12 to 1.26, respectively.

4.2.4. Neonatal ejection fraction (EF), stroke volume (SV) and cardiac output (CO)

The EF measured according to the Simpson method was similar in the LV even after birth (63.58% compared to 64.66% in fetuses), the RV-EF (55.51%) was significantly lower compared to the EF in fetuses and even compared to LV measurements postnatally ($p < 0.001$). After birth, SV and CO measurements were only performed in the LV and were similar to the combined SV and CO in fetal life (SV = 6.27 ml and CO = 797 ml/min after birth, combined SV = 5.51 ml and CO = 764 ml/min in fetuses).

When related to birth weight, CO was 232 ml/kg/min and SV 1.8 ml/kg. No fetal weight estimates were performed.

The correlation between 2D-S measurements and conventional echocardiography was good concerning EF by Simpson-planimetry ($p = 0.01$) and in the M-Mode ($p = 0.03$), in comparison with Doppler-derived methods, the correlation was acceptable but not significant ($p = 0.08$).

Table 4
Stroke volume (SV in ml), cardiac output (CO in ml/min), EF (%) by planimetry and myocardial performance index (MPI), relation between max. velocities in early diastole in pulsed Doppler (E) and 2D-S (E′) and relation between early and late diastolic max. velocities in pulsed Doppler (E/A) and 2D-S (E′/A′) for the right (RV) and left ventricle (LV) in echocardiographic examinations at 28th week of gestation (fetal) and after birth (neo).

	Fetal		Neo	p-Value[a]
RV	SV (ml)	3.25 (3.00–3.51)	–[b]	–
	CO (ml)	443 (421–465)	–[b]	–
	EF (%)	65.29 (62.6–68.0)	55.51 (53.1–58.4)	<0.001
	MPI	0.26 (0.20–0.33)	0.17 (0.11–0.22)	0.01
	E/E′	11.3 (8.8–13.7)	8.7 (6.9–10.4)	0.07
	E/A	0.88 (0.76–1.00)	1.00 (0.78–1.21)	0.66
	E′/A′	1.12 (0.76–1.48)	1.26 (1.04–1.49)	0.48
LV	SV (ml)	2.26 (2.1–2.43)	6.27 (6.18–6.39)	–
	CO (ml)	321 (300–342)	797 (777–810)	–
	EF (%)	64.66 (61.5–67.9)	63.58 (62.0–66.6)	0.57
	MPI	0.26 (0.21–0.31)	0.26 (0.21–0.30)	0.67
	E/E′	11.5 (8.7–14.4)	11.8 (9.6–14.1)	0.67
	E/A	0.91 (0.75–1.08)	1.11 (1.00–1.22)	0.12
	E′/A′	1.06 (0.91–1.20)	1.48 (1.21–1.75)	0.005

[a] Data are mean (SD), p-values according to paired *t*-test.
[b] Measurements not performed.

5. Discussion

Transition from fetal to neonatal life involves important cardiac and hemodynamic processes, which according to our findings can be assessed by the novel technique of speckle-tracking echocardiography,

an apparently feasible and reproducible tool for the evaluation of cardiac function in fetuses as well as in newborns.

The major result of this study represents an important change in myocardial function in the transitional period from fetal to neonatal life, illustrated by a highly significant decrease in longitudinal strain and strain rate and increased myocardial velocities after birth. To our knowledge, this is the first report analyzing these myocardial functional changes in a healthy and homogenous population of infants by the use of speckle-tracking technique.

The cardiopulmonary transitional processes from fetal to neonatal life are multiple and complex. The combination of the closure of fetal shunts and the changes in cardiac output as well as in systemic and pulmonary preload, afterload and resistance make it difficult to interpret speckle-tracked results, since the majority of all measured parameters seem to be load-dependent.

Preload increases after birth as a result of a less restrictive ventricular function due to the change in pericardial pressure, which is higher in the intrauterine cavity across the thorax and fluid-filled lungs. This pressure decreases when negative intrapleural pressure after lung expansion occurs, a process that leads to a less restrictive ventricular filling pattern. This phenomenon is illustrated by the E/A-conversion after birth in both chambers. The left ventricular preload is mainly dependent on pulmonary blood flow and venous return to the left atrium. Since pulmonary resistance continuously falls after birth and pulmonary blood flow increases, it is reasonable that left ventricular preload rises. Data for right ventricular preload are less conclusive, but it seems that preload drops when clamping the umbilical cord and rises within hours to supra-fetal levels.

The effect of higher preload towards strain, strain rate and velocities has been discussed controversially: in one study [16], which analyzed right ventricular measurements after the percutaneous closure of an atrial septal defect, the authors could show that strain and strain rate were rather load-independent, whereas myocardial velocities were significantly higher before the closure, and normalized afterwards. In another study, Burns et al. [17] found that a decrease in preload by the administration of glyceryl trinitrate led to higher strain and strain rate values. Even in abrupt changes provoked by parabolic flight [18], reduced preload was associated with reduced velocities in the myocardium.

Secondly, arterial blood pressure as a proxy for left ventricular afterload increases postnatally [19]. Carasso et al. [20] could find that a significant increase of afterload caused by severe aortic valve stenosis was associated with lower longitudinal and higher circumferential strain. After operative valve replacement, longitudinal strain rose and circumferential strain decreased. Even outside of this study, patients with systemic arterial hypertension and pathological strain measurements exhibited higher myocardial velocities and higher strain rates when treated with Valsartan in order to reduce blood pressure and afterload [21]. In the above-mentioned study by Burns et al. [17], saline fluid infusion to higher afterload contributed to lower strain and strain rate measurements. In patients after a Senning procedure who are exposed to unusual systemic right ventricular afterload, right ventricular strain was significantly reduced in comparison to the healthy controls [22].

These data are quite comparable to our measurements, as we found lower strain and strain rates in association with higher myocardial velocities in neonates with an increased afterload compared to fetal conditions. However, this may be only quite true for the left ventricular afterload. As pulmonary resistance decreases and pulmonary blood flow increases, right ventricular afterload might be lower than in the fetal condition.

Inotropic stimulation in the animal model [23] and in vitro [24] showed clear effects on strain and strain rate measurements. In general, catecholamine administration contributed to higher strain and strain rate values. It is well known that catecholamine levels are extremely high directly after birth as a consequence of delivery stress, but fall to lower levels during the early postnatal adaptive period. As we examined the infants an average of 170 h after birth, catecholamine concentrations may have dropped and the positive effect on myocardial contraction might be therefore less pronounced. Unfortunately, our study protocol did not allow us to take blood or urine samples in order to quantify the sympathoadrenergic effect on speckle-tracking measurements.

In addition to load-dependency, another possible explanation for our findings is the fact that cardiomyocytes do not divide to the same degree in the postnatal period, and that cardiac growth mainly occurs via myocardial hypertrophy. This phenomenon is also reflected by the DNA/protein ratio, which falls significantly after birth. Therefore, postnatal growth is associated with a decrease in strain and strain rate as the absolute number of contractible myocytes decreases in relation to heart volume. This appears to occur directly after birth and does not necessarily affect myocardial velocity, which is demonstrably higher after birth.

Strengths of the present study include the prospective inclusion of a healthy study population and its longitudinal design. We used established techniques for conventional echocardiography and achieved high quality images in the two-dimensional projections with high frame-rates, which enabled reproducible off-line analyses in all examinations. There are limitations as well: the study group was relatively small and occasions of ultrasound investigations limited to the 28th week of gestation and one week after term delivery. However, no data is available for the period between both examinations. Nevertheless, other studies indicate that velocity parameters increase during the third trimester of gestation, whereas strain and strain-rate values decrease. This is consistent with continuously increasing afterload in this period and in line with our observation after birth. Additionally, as in all fetal studies, dummy ECG is used to define heart cycles. This can only be an approximation to the ECG used postnatally.

Another important limitation is the use of software that was developed for the analysis of the left ventricle in an adult population, and that it is not self-evident that the obtained measurements reflect real displacement and deformation modalities in smaller ventricles and even on the right side of the heart. However, ventricular tracing techniques were manually adapted to the right ventricular anatomy as adequate as possible, and safe discrimination of regions of interest even in the fetal heart was not a problem.

In fact, the assessed measurements for strain, strain rate and tissue velocities were very much reproducible and in accordance with other studies using the same ultrasound instruments and algorithms for strain calculations in fetuses [2,8,9]. These studies applied speckle-tracking technique at different gestational ages. Di Salvo found an increase in peak systolic strain whereas Ta-Shma reported unchanged strain, increased tissue velocities and decreased segmental and global strain rate during gestation. Other research groups using vector velocity imaging (VVI) [1,4–7,12,15] found lower values for strain, strain rate and velocity, pointing to the fact that the evaluation of fetal cardiac function is probably not comparable between different ultrasound systems.

In addition, our postnatal results are very much in accord with another study by Pena et al. [25] using color Doppler-derived strain and strain rate values in newborns at 20 h and at 30 days of age. Interestingly, they found a decrease of left ventricular strain and systolic strain rate in the basal and apical segments of the lateral wall due to an increase in afterload at the second examination. Accordingly, lower right ventricular afterload resulted in an increase of systolic strain and strain rate in the basal, mid and apical segments of the right ventricular free wall. Even these results confirm our hypothesis about how hemodynamic changes in the transitional period from fetal to postnatal life alter values of speckle-tracked strain and strain rate.

As a result of changes in preload, afterload and inotropy, cardiac output changes after birth and is almost identical in the right and left chamber due to the serial arrangement of circulation. Our

measurements of cardiac output post-partum are comparable to recent data from a functional cardiac magnetic imaging study by A. Groves [26] (232 ml/kg/min vs 245 ml/kg/min), and similar to studies performed by conventional echocardiography [27,28] (232 ml/kg/min vs 236 and 231 ml/kg/min respectively).

Our fetal measurements of cardiac output, too, are consistent with the results of a study by M. Mielke [29] using the same technique as in this study.

In conclusion, speckle-tracking is apparently a feasible and reproducible technique in analyzing both fetal and newborn cardiac functions and might contribute to new insights in transitional physiology. In addition, 2D-S technique is relatively easy to learn, and post-processing time has considerably decreased with the newer automated systems. Therefore, the speckle-tracking technique might be useful in clinical examinations of fetuses and newborns. Further prospective studies that include large numbers of infants with pathological hemodynamic conditions are required in order to evaluate the prognostic value of the novel parameters.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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