Variations in ductus arteriosus Doppler parameters in different sonographic views during the second half of gestation

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Abstract. The aim of the present study was to compare the Doppler parameters of the fetal ductus arteriosus (DA) measured in the traditional longitudinal ductal arch (LDA) view and the newly introduced three vessels and trachea (3VT) plane of the fetal upper mediastinum. The peak systolic velocity (PSV), end-diastolic velocity (EDV), time-averaged maximum velocity (TAMXV) and velocity-time integral (VTI) measurements were taken for 52 fetuses with normal growth (including 29 females). The pulsatility index (PI) and resistance index (RI) were calculated. All parameters for each fetus were measured three times by the same sonographer in the LDA and the 3VT view, and the averages were taken to obtain the final value. Differences in the above values obtained from the LDA and 3VT views were analyzed and the correlation between the differences of all indices and the gestational age (GA) was evaluated using Pearson's linear coefficient of correlation. All of the values were characterized as normally distributed continuous variables by homogeneity of variance analysis. Slight increases in the PSV, EDV, TAMXV and VTI determined in the LDA view were identified compared with those in the 3VT view ($P<0.05$). Furthermore, these increases were identified to be independent of the GA ($P>0.05$). However, no significant differences in the impedance indices PI and RI were observed between the two sonographic planes ($P>0.05$). In conclusion, the LDA view provides a better chance than the 3VT view to obtain higher values of velocity parameters (PSV, EDV, TMAXV and VTI) within the fetal DA, and the differences are independent of the GA. However, no significant variations in the impedance indices PI and RI were observed between these two sonographic planes.

Introduction

The ductus arteriosus (DA) is an important component of the fetal cardiovascular system. In the normal fetal circulation, the DA diverts ~78% of the right ventricle output or 46% of the combined cardiac output away from the non-ventilated lungs and joins the descending aorta to supply the lower body (1,2). Furthermore, as an important pathway between pulmonary and systemic circulations, the DA has a vital role in modulating the flow distribution between the left and right side of the heart to support the development of important organs, even in the case of congenital heart disease (CHD) (3,4). The hemodynamic status of the DA is a major factor that is being considered in the prenatal diagnosis of CHD and decision-making regarding its management (5).

Spectral Doppler sonography is widely used in the clinic due to its reliability in providing quantitative data for the comprehensively antenatal evaluation of fetal DA. In general, two sonographic views are independently used to obtain the flow waveforms of fetal DA, namely the traditional longitudinal ductal arch (LDA) view or the new introduced three vessel and trachea (3VT) view. However, it remains controversial which of the two sonography views is superior in the evaluation of fetal DA, and differences in the values of velocity parameters measured using these two views have been noted by numerous specialists in fetal cardiology (6-10). To address these limitations in knowledge, a detailed study was performed to confirm whether sonography assessment from the LDA and 3VT views indeed provides different Doppler parameters of the fetal DA. Furthermore, the present study aimed to determine the exact differences and their potential correlation with the gestational age (GA).

Patients and methods

Study population. In the present study, fetuses referred to the Center for Medical Ultrasound of the Affiliated Hospital of Nanjing Medical University (Suzhou, China) for routine screening for fetal CHD from May 2017 to June 2017 were

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enrolled. The Ethics Committee of the Affiliated Suzhou Municipal Hospital of Nanjing Medical University approved this study, and all pregnant subjects provided their written informed consent.

The fetal GA was determined based on the time-point of the last menstruation of the mother. If this information was not available, the fetal GA was estimated according to the combination of abdominal circumference, femur length and biparietal diameter obtained by sonography. The criteria for inclusion were as follows: i) Absence of congenital malformations and intrauterine growth retardation revealed by routine ultrasound screening in obstetrics, ii) normal anatomy, diameter and flow supply of the fetal DA, iii) normal fetal heart rate (120-160 bpm) and rhythm, iv) low risk for aneuploidy suggested by cell-free fetal DNA testing, v) absence of maternal conditions potentially affecting fetal hemodynamics.

Ultrasound equipment. Fetal echocardiography was performed according to the American Society of Echocardiography guidelines (11), using a Voluson E8 ultrasound system (GE Healthcare Ultrasound, Milwaukee, WI, USA) coupled with a 3.5 MHz curved-array transducer.

Standardized technique. A standard protocol on waveform recording and measurement of parameters for detecting fetal DA was used for each fetus. First, routine obstetric ultrasound scanning was performed to exclude the presence of congenital malformations, fetal intrauterine growth retardation and abnormal placental function. Subsequently, the normal anatomy, diameter and flow supply of the fetal DA was confirmed from the LDA and 3VT views. In particular, the 3VT view was obtained at the level of the fetal upper mediastinum by moving the transducer cranially to maintain a transverse position from the four-chamber view, as described by Yagel *et al* (12). The characteristic V-shape to the left of the fetal trachea in 3VT view represented the convergence of the aortic isthmus and DA, and the LDA view was obtained by slightly tilting the transducer from the right ventricular outflow tract (RVOT) view until the RVOT, major pulmonary artery trunk and DA were aligned in the shape of a 'hockey stick-like' line (13). The flow waveform of fetal DA in the LDA and the 3VT view was then separately obtained by using a pulsed wave, ensuring that the fetus had no obvious breathing movement during the Doppler sampling, and the sampling point was placed at the middle point between the origin of the left pulmonary artery and the beginning of the descending aorta.

To standardize the reproducibility and accuracy of the measurements, machine settings included the following: i) A high frame rate with increased contrast and high resolution, ii) a high-pass wall motion filter (50 Hz) and low-energy output levels (<50 mW/cm^2), iii) absence of Doppler aliasing and iv) an angle of insonation as close to 0˚ as possible (<15˚). In a continuous attempt to minimize the measurement and observation biases, flow waveform obtainment and tracing were evaluated by the same experienced fetal echocardiography specialist. Furthermore, to minimize intra-observer variations, the average of three repeated measurements under the same conditions taken as the final value. The peak systolic velocity (PSV), end-diastolic velocity (EDV), time-averaged maximum velocity (TAMXV) and velocity-time integral (VTI) in the two views were recorded for post-processing (Fig. 1). The pulsatility index (PI) and resistance index (RI) were calculated according to the following formulas: PI=(PSV-EDV)/TAMXV and RI=(PSV-EDV)/PSV (14).

Table I. Demographic data for all subjects.

Item	Value
Maternal age (years)	31.5 (23-37)
Gestational age (weeks)	31.7 (21-39)
Fetal heart rate (bpm)	141 (112-157)
Fetal biometry (mm)	
BPD	81 (50-95)
AC	275 (160-350)
FL	61 (35-76)
Cell-free fetal DNA testing (z-score)	
Trisomy 21	0.23 (-0.07-0.42)
Trisomy 18	-0.59 (-1.19-0.27)
Trisomy 13	-0.24 (-0.89-0.43)

Values are expressed as the mean (range). AC, abdominal circumference; FL, femur length; BPD, biparietal diameter.

Statistical analysis. Statistical analysis was performed with SPSS version 19 for Windows (IBM Corp., Armonk, NY, USA). The entirety of the data was checked for normality of distribution using the Kolmogorov-Smirnov test and for homogeneity of variance with Levene's test. Normally distributed continuous variables were expressed as the mean ± standard deviation or range. The significance of differences in PSV, EDV, TAMXV, VTI, PI and RI of the DA between the LDA and 3VT views was assessed using unpaired Student's t-tests. Bland-Altman plot analysis was used for illustrating differences in the impedance indices PI and RI. Correlations between differences in all indices and the GA were evaluated by calculating Pearson's linear coefficient of correlation. P<0.05 was considered to indicate a statistically significant difference.

Results

Basline characteristics. During the study period, satisfactory flow waveforms of the fetal DA were successfully obtained in the LDA and 3VT sonographic planes for 52 normal singleton fetuses (23 males and 29 females). The demographic features are presented in Table I. The mean maternal age at the time-point of the sonography scan was 31.5 years (range, 23-37 years), and the mean GA was 31.7 weeks (range, 21-39 weeks). The mean fetal heart rate was 141 bpm (range, 121-157 bpm). The mean fetal biparietal diameter, abdominal circumference and femur length were 81 mm (range, 50-95 mm), 275 mm (range, 160-350 mm) and 61 mm (range, 35-76 mm), respectively. Cell-free fetal DNA testing of all subjects revealed low risks for trisomies 21, 18 and 13.

Differences of Doppler parameters. The parameter values were continuous variables and normally distributed according

Table II. Doppler parameters of fetal ductus arteriosus measured at the 3VT and LDA views (n=52).

	LDA		3VT		
Parameter	Mean ± SD	Range	Mean ± SD	Range	P-value
PSV	94.49±17.59	62.80-155.00	90.66±16.98	59.00-143.00	<0.01
EDV	11.33±1.77	7.80-14.10	11.11±1.80	7.60-14.10	<0.01
TAMXV	33.27±6.20	22.30-53.30	31.93±6.38	19.10-48.10	0.01
VTI	13.79±2.76	8.27-22.10	13.24±2.92	7.75-21.30	0.02
PI	2.50±0.27	2.07-3.21	2.50±0.27	2.07-3.08	0.99
RI	0.88±0.17	0.85-0.92	0.88±0.21	0.82-0.92	0.10

PSV, peak systolic velocity; EDV, end diastolic velocity; TAMXV, time-averaged maximum velocity; VTI, velocity-time integral; PI, pulsatility index; RI, resistance index; SD, standard deviation; 3VT, three vessels and trachea; LDA, longitudinal ductus arch.

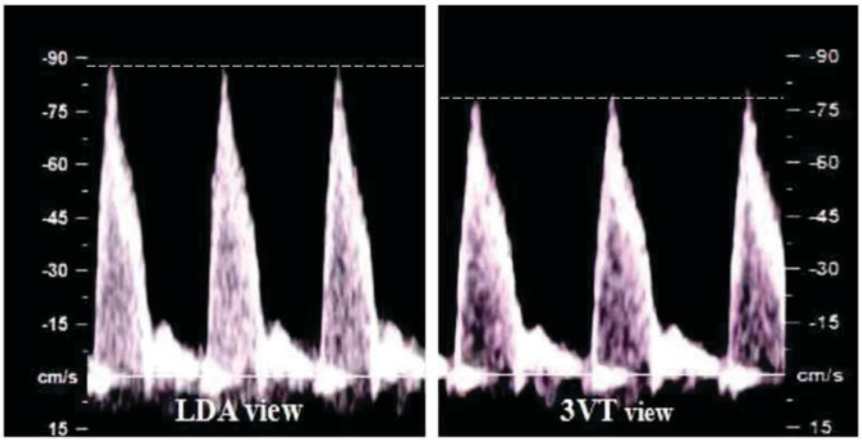

Figure 1. Doppler velocity waveforms of the ductus arteriosus obtained in the LDA and 3VT views of a fetus at 32 weeks of gestation. LDA, longitudinal ductal arch; 3VT, three vessels and trachea.

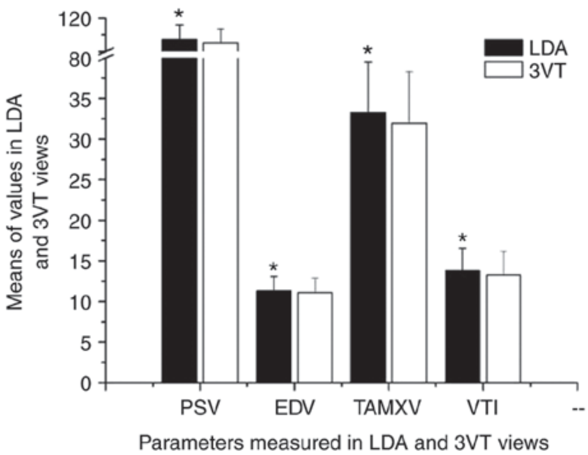

Figure 2. Variations in velocity indices in the LDA and 3VT views. *P<0.05 vs. 3VT. PSV, peak systolic velocity; EVD, end-diastolic velocity; TAMXV, time-averaged maximum velocity; VTI, velocity-time integral; LDA, longitudinal ductal arch; 3VT, three vessels and trachea.

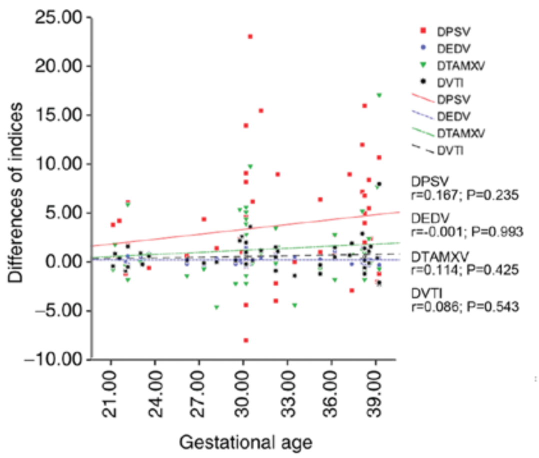

Figure 3. Correlation between differences in all indices and gestational age. DPSV, difference of peak systolic velocity; DEVD, difference of end-diastolic velocity; DTAMXV, difference of time-averaged maximum velocity; DVTI, difference of velocity-time integral.

to the homogeneity of variance analysis. The PSV, EDV, TAMXV and VTI measured in the LDA view were significantly increased compared with those measured in the 3VT view (P<0.05; Table II and Fig. 2). Furthermore, no significant correlation was identified between these parameters and fetal GA, which means that the differences in velocity parameters measured in the LDA and 3VT views were independent of the GA (P>0.05; Fig. 3). However, no significant differences in the impedance indices PI and RI were identified between the LDA view and 3VT view (P>0.05; Table I). The Bland-Altman analysis demonstrated the agreement of RI and PI measured in two different views (Figs. 4 and 5).

Discussion

Quantitative analysis of the fetal DA hemodynamics has an important role in the comprehensive antenatal evaluation of the fetal cardiovascular function, particularly in those fetuses with DA-dependent CHD. The accuracy and reliability of sonographic parameters are affected by numerous factors, including the sonographic view used for data measurement or calculation. The present study revealed differences in the parameter values obtained from the LDA and 3VT views, while the two have been widely used in previous relevant studies. Specifically, the present study revealed a slight increase in the PSV, EDV, TAMXV, and VTI obtained in the LDA view compared with those obtained in the 3VT view, and that those increases are not correlated with the GA. However, no significant differences in PI and RI were observed between the two sonographic planes. The possible explanations for this phenomenon are further discussed below.

The angle between fetal DA and the ultrasound beam is the key factor affecting the differences in Doppler measurements between the LDA and 3VT views. The LDA view has a greater probability than the 3VT view to form a smaller angle or even a parallel alignment of the central axis of the bloodstream flowing through the DA and the ultrasound beam. First, it is well-known that the fetal DA and aortic arch are not at the same horizontal level of the fetal body (15,16); in fact, the DA is situated slightly lower than the aortic arch, which can be verified by the earlier emergence of DA compared with the transverse arch when sliding the transducer cranially from the four-chamber plane towards the fetal upper mediastinum (17). The central axis of the lumen of the fetal DA, where the blood flow is fastest, is not included in the 3VT view where the classic 'V-like' sign is formed by the pulmonary artery and the aortic arch, and the DA seen from the 3VT view is actually the upper part of the fetal DA lumen. Furthermore, physiologically, the angle between the DA and the descending aorta (DAO, 98.4±12.5˚) is significantly larger than that between the aortic arch and the DAO (88.5±5.5˚) (18-20). Since the 3VT view is obtained in the horizontal direction of the fetal body, the angle between the DA and DAO is relatively large, thereby reducing the probability of forming the smallest angle between the DA and the ultrasound beam compared with that including the aortic arch. However, in the LDA view, the sagittal section of the DA arch was clearly visualized in a 'hockey stick' shape (13). The transducer may be slid in any direction to obtain the smallest angle between the DA flow and ultrasound beam regardless of the spatial association with the aortic arch and the DAO. Therefore, compared to the 3VT view, the LDA view allows for achieving a smaller angle between the DA and the ultrasound beam. Therefore, higher velocity parameters of fetal DA may be measured in the 3VT view. However, there were no differences in the PI and RI calculated in the two views, which was consistent with the well-known theory that the impedance indices are independent of the sampling angle of the target structure and ultrasound beam.

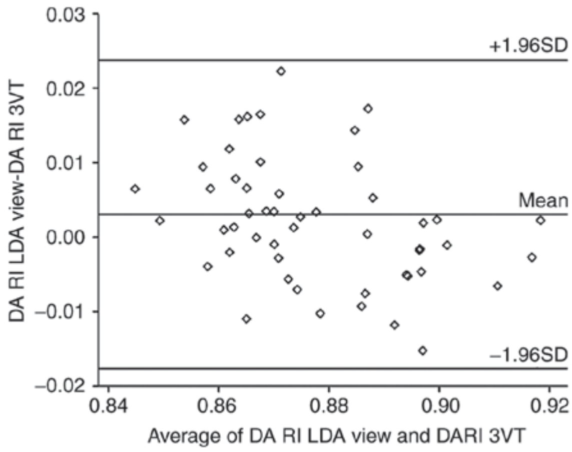

Figure 4. Bland-Altman plot of the difference vs. the average of the DA RI in the LDA and 3VT views. SD, standard deviation; DA RI, ductus arteriosus resistance index; LDA, longitudinal ductal arch; 3VT, three vessels and trachea.

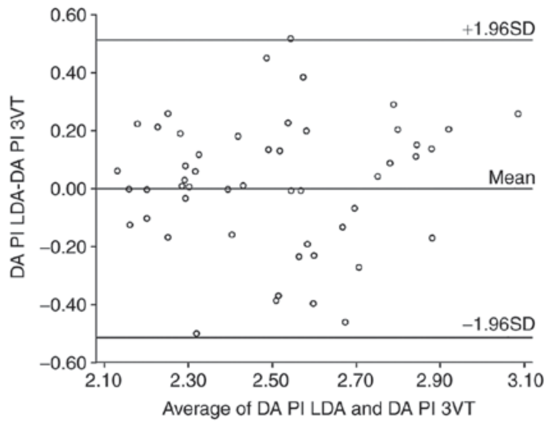

Figure 5. Bland-Altman plot of the difference vs. the average of the DA PI in the LDA and 3VT views. SD, standard deviation; DA PI, ductus arteriosus pulsatility index; LDA, longitudinal ductal arch; 3VT, three vessels and trachea.

The present study revealed that the velocity parameters of the fetal DA measured in the LDA view are significantly higher than those obtained in the 3VT view, and the differences are independent of fetal GA. This means that in the second half of gestation, the LDA view is better than the 3VT view in the assessment of the flow restriction or the tendency of premature closure of fetal DA. In addition, the present study also demonstrated that the impedance indices PI and RI of the flow within the fetal DA are similar between the LDA and 3VT views. In other words, it is not necessary to obtain the LDA view, as is performed for the measurement of velocity parameters, if only the impedance indices of the fetal DA are required.

The primary limitations of the present study were as follows: First, the relative spatial associations among the fetal DA, aortic arch and DAO may vary with advancing gestation, which was not taken into consideration in detail. Of note, most obstetric ultrasound screening examinations are performed during the second half of gestation. Furthermore, the present study did not include any fetuses with premature restriction, closure of the DA or arteriosus aneurysm. In those cases, it is required to slightly adjust the transducer to identify the smallest angle between the DA and ultrasound beam to obtain the optimal waveform, which were not usually in the standard LDA or 3VT views.

In conclusion, the LDA view has a greater probability than the 3VT view to obtain higher values of velocity parameters of the fetal DA, including PSV, EDV, TMAXV and VTI, and the differences are independent of the fetal GA. However, no significant variations were observed in the impedance indices PI and RI between these two sonographic planes.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

ZG conceived of the study, collected the data, acquire funding and wrote the manuscript. JZ, ZW and SL collected the data. XY analyzed the data and wrote and edited the manuscript. ZG, XY, JZ, ZW and SL designed the study. XD acquired funding and performed the experiments.

Ethics approval and consent to participate

The Ethics Committee of the Affiliated Suzhou Municipal Hospital of Nanjing Medical University approved this study. All pregnant subjects provided their written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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