**Original Investigations**

# Reference ranges for the flow velocities and the indices of the ductus venosus in low-risk pregnancies

**Gürses et al. Ductus venosus blood velocities**

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**Abstract**

**Objective:** Ductus venosus blood flow velocity measurements are mandatory in many clinical indications. The evaluation of the flow is performed either by comparing the results with the reference tables or by checking the “a” flow qualitatively as reversed or absent in the spectral waveforms.
It is aimed to develop the normal reference ranges in low-risk pregnancies of our population.
**Material and Methods**: Measurements of flow velocities (S, v, D, a) and indexes (PIV, PVIV, a/S, S/a) were performed by a single experienced specialist in 1279 singleton uncomplicated pregnancies between 11 and 40 weeks. The absolute flow velocities (S, v, D, a, Vm_Peak) and indexes (PIV, PVIV, a/S, S/a) are obtained from the spectral waveforms using the equipment producer’s preset system. The still images were stored in the picture archiving and communication system.
**Results:** The predicted reference ranges of the DV blood flow velocities according to the gestational age are shown in tables and graphics. Predicted reference curves based on the 5th and 95th percentiles according to gestational week were plotted and given in tables and figures.
**Conclusion:** The normal reference ranges for absolute flow velocities and indexes were studied in a tertiary care center. The measurements are performed by a single operator, a specialist certified by FMF, either in the classic patterns of the waveforms, about which there

are several studies or in case of the variants of the spectral waveforms, which was published recently, for the first time in the medical literature.
**Keywords:** Doppler, ductus venosus, ultrasonography

## Introduction

Ductus venosus (DV) Doppler assessments play a critical role not only for the diagnosis of chromosomal abnormalities and congenital cardiac defects in early pregnancy but also for determining cardiovascular health in the follow up of the pregnancy. It is suggested to be used for surveillance and timing of delivery in the UK (1).
DV spectral waveform pattern has two peaks (S & D) and two nadirs (v & a) in a cardiac cycle. "S" and "D" peaks correspond to the maximum and "v" and "a" nadirs correspond to the minimum intra-atrial pressure, which accelerates or decelerates the forward flow in DV throughout a cardiac cycle (Fig. 1-7, Vid. 1-3). The flow in DV is assessed by either qualitatively observing the spectral pulsed Doppler (PD) flow checking the "a" nadir in the waveform as "reversed" or "not" and or quantitatively comparing the measurements with the reference ranges for each week of the pregnancy published in the medical literature (2-5).
Even though there are some studies to establish the reference values, advancing technologies to visualize the ductus venosus and obtaining the reproducible measurements are easier and the updated limits seem to be necessary. We aimed to derive reference ranges of angle depended on absolute flow velocities for S, v, D, a and Vm_Peak which have two peaks and two nadirs during a cardiac cycle and the angle independent Doppler indices of pulsatility index for veins (PIV), peak velocity index for veins (PVIV), a/S, S/a, preload index [(S - a) / S)] (6, 7), SIA index [S / (v + a)] (8) (Fig. 1).

## Material and Methods

A total of 1279 singleton low-risk pregnancies fulfilling the inclusion criteria below, which mean a pregnancy as either uncomplicated or without the factors that might threaten the maternal and fetal safety, between 11 and 40 weeks were included in this prospective study between January 2016 and February 2018.
The written informed consent from the patients and the ethical approval from the Institutional Review Board (02.11.2017, 16 / 13) were obtained.
Measurements of DV flow velocities (S, v, D, a, Vm_Peak) and indexes (PIV, PVIV, a/S, S/a) were performed using a spectral waveform. Isovolumetric relaxation velocity (IRV or DV v) was measured manually since it was not included in the equipment producer's preset measurement system. The preload and SIA indexes were calculated using Microsoft Excel (Microsoft, 2007; Microsoft Corp., Santa Rosa, CA, USA).
DV measurements were performed in all variants of the spectral waveform patterns of the DV flow, which were described recently by Gürses et al (9), and the calculations were either in normal component of type 4 or type 5 flows or after the flow pattern turn to the classic pattern either in type 6 or 7 of the flow pattern.
Fetal age was estimated according to the last menstrual period. However, in case of discordance of more than 7 days between the age based on the last menstrual date and the age based on the biometry measures with ultrasonography, the gestational age was redated.
Patients are included in these circumstances; (1) cases with optimal visualization of the DV using a wideband color Doppler technique (advanced dynamic flow), (2) Apgar score ≥ 8, (3) Fetal weight ≥ 2500 grams, (4) measurements in a single optimal waveform after obtaining 4 to 5 consecutive uniform Doppler velocity waveforms in the tracings with 2-3 cm/s sweep speed, (5) patients with normal amniotic fluid index, (6) patients with normal screening tests.
Patients are excluded in these maternal and fetal situations; (1) gestational diabetes, (2) multiple pregnancies, (3) preeclampsia, (4) maternal cardiac rhythm disturbances, (5)

smoking, (6) polyhydramnios or oligohydramnios, (7) fetal morphological abnormality, (8) intrauterine growth restriction, (9) macrosomia, (10) fetal stillbirth, (11) Apgar score < 8 newborns, (12) fetuses with transient bradycardia (deceleration).

Doppler examinations are performed by a single experienced specialist (C.G.), certificated for DV flow and Doppler examinations by Fetal Medicine Foundation (FMF ID: 127129), (137 Harley Street, London, W1G 6BG, United Kingdom). DV measurements are performed according to the criteria in the medical literature (10-13). The 1 mm wide sample gate is positioned over the isthmus and adjacent proximal section, where the aliasing occurs due to the accelerated jet flow. The wide-band color Doppler technique (Advanced Dynamic Flow) was used for mapping the DV and placing the sample gate accurately in pulsed Doppler examinations to avoid contamination from the adjacent veins during the pulsed Doppler tracings (Fig. 2-7, Vid. 1-3).

The still images were stored in the Sectra PACS (picture archiving and communication system) system (Sectra AB, Teknikringen 20, SE-583 30 Linköping, Sweden).

Toshiba Applio 500 system (TUS-A500, Toshiba Medical Systems Europe B.V., Zilverstraat 1, 2718 RP, Zoetermeer, The Netherlands) is used in all examinations with a 2–6 MHz broadband convex transducer.

The acoustic output level was adjusted to a minimum following the ALARA principle and the maximum mechanical index was 1,1. Imaging parameters were calibrated as the dynamic range (DR) 70, dynamic frequency (DF) 3.0, and color gain (CG) 40, color PRF 5-6 and color filter (F) 3-4. Sweep speed was 2-3 cm/s in all of the trimesters and the Doppler filter was set between 90 and 140 in the first trimester of the pregnancy during the pulsed Doppler examinations.

**Statistical analysis**

Data were collected using Microsoft Excel for Windows (Microsoft, Redmond, WA, USA) and the analysis was performed using the Statistical Software for Social Sciences for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA). Data are presented as mean ± SD. For the statistical analysis, the distribution of each blood flow velocity and DV index was examined using scatter plots against the gestational age. Because of the descriptive nature of the study, no tests of statistical significance were performed.

**Results**

A total of 1279 singleton pregnancies between 11 and 40 weeks were enrolled in this prospective, cross-sectional study. The peak forward velocities were recorded and the DV indices were calculated (Fig. 1-7). The mean maternal age was 28.05±6.54 year and the mean birth weight was 3294 ± 448,5 g. The median gestational age was 22 weeks (range 11 to 40) and the mean body mass index was 29,05 ± 5,17. The average number of participants for each week of gestation was 35, ranging from 23 to 86.

The predicted reference ranges of the DV blood flow velocities and indices according to the gestational age are shown in Table 1-6. Predicted reference curves based on the 5th and 95th percentiles according to gestational week were plotted and given in figures (Figs. 8-10).

**Discussion**

Since the ultrasonographic velocimetry of the fetal DV is described by Kiserud et al (14) for the first time, the several studies related to the reference ranges of either the absolute flow velocities, which are the insonation angle-dependent or the indices, which are preferred in clinical practice due to being the insonation angle-independent measurements has been created for the whole weeks of the pregnancies (2-5, 15).

Doppler assessment of the DV should satisfy some criteria, which are depicted in detail in the medical literature (10-13). In our study, these criteria were constant in a user preset adjustment and additionally the wideband color Doppler technique, in which blooming is thought to be less than the conventional narrowband technique was used to image the DV and to place the sample gate before performing measurements. Blooming is one of the color Doppler artefacts and causes vessels larger than the actual diameters due to the reaching of color beyond the vessel walls. Blooming artefact is the main restrictive disadvantage to the visualization of the vascular territories due to the lack of lateral discrimination and it causes exaggerated or false positive vascular colorizing (16, 17). Blooming has unique importance for the tiny or slow-flow blood vessels of the fetus. Blooming increases not only false vascularity but also wrong placement of the sample gate in PD tracings and causes prolonged examination time. Maiz et al demonstrated that a sonographer needs to perform an average of 80 examinations to achieve competence in the Doppler assessment of the DV. One of their criteria is to get measurements in a right ventral mid-sagittal view (10). However, it is thought that the main point is to get the blood flow direction to be towards the transducer plane so therefore to achieve the insonation angle close to 0 (Fig. 1, Vid. 1) and the wideband color Doppler technique allows visualizing the intrahepatic UV, the LPV and the PS not only in ventral but also in dorsal approach (Fig. 1, Vid. 1).

Even though the sample volume is suggested to use 2-5 mm wide in the second half of the pregnancy by Martins and Kiserud (13), in the present study the 1 mm wide sample gate were used in every week of the pregnancies to be either comparable of the velocities with the results of the previous weeks of pregnancy or to avoid flow contaminations of hepatic veins and inferior vena cava.

Despite the difficulties in obtaining the insonation of the vessel at a 0-degree angle in some cases, the absolute flow velocities were measured in DV at 0 or close to 0 in most of the cases or at least under the 30 degree of insonation in the present study. The wideband color Doppler technique was quite helpful to determine the actual blood flow direction, so thereby deciding the angle of insonation. DV absolute flow velocities are increased in anaemia and diseases affecting the liver parenchyma (18, 19) and the angle of insonation has essential importance for the absolute flow velocity measurements in DV. In the present study, the angle independent indices such as pulsatility index for veins (PIV), peak velocity index for veins (PVIV), a/S, S/a were measured simultaneously with the absolute flow velocities by the preset software of the equipment producer. The flow is maximum in velocity when the atrial pressure is minimum in “S” and “D” peaks during ventricular systole and early ventricular diastole, respectively (Fig. 1) and the flow is the minimum in velocity when the atrial pressure is maximum in “v” and “a” nadirs during end-systolic ventricular relaxation and atrial systole (Fig. 1) (7). In daily practice, the PIV is clinically the most widely utilized (7). However, PIV is thought to give an incomplete reflection of cardiac function, since relative changes in v- and D-wave velocities are not well reflected (15) (Fig. 1).

The afferent system of the fetal precordial venous system includes the intrahepatic umbilical vein (UV), the left portal vein (LPV), the DV, the right portal vein (RPV) and the main portal vein (MPV). The portal sinus (PS) is the L-shaped confluence of the LPV and RPV (20, 21, 22). DV arises from the PS just before turning at an almost right angle to the right (Figs. 11-12) to create the pars transversa of the PS and DV connects the LPV to the subdiaphragmatic vestibulum of the inferior vena cava, where the left and middle hepatic veins connect additionally (21, 22). Maternal oxygenated blood in the LPV is shunted through the DV and directed towards the left atrium via the foramen ovale (18-20). DV is an essential component of the classical “via Sinistra” pathway (22) and thus the myocardium and cerebral circulations receive more oxygenated and higher nutritional blood from the placenta.

Blood flow velocities of the DV in a cardiac cycle change according to the weeks of pregnancy because of some physiologic properties of the fetal circulation. For example, the human DV at 13-17 weeks of gestational age has novel structural features distinct from those of other blood vessels (23) or the umbilical blood flow decreases with gestational age and at 28 to 32 weeks, the shunting through the DV reaches the minimum (22, 24) or the fraction of combined cardiac output directed to the placenta reduces after 34 weeks (24). The study population is important when establishing reference ranges of the blood flow velocities of the DV (25). The most difficult period to measure the patients was towards the end of pregnancy, especially between 38 and 40 weeks, since the per cent of the caesarean delivery is more than the vaginal way, unfortunately.

There are some limitations in the present study. The number of patients for each week of pregnancy is different since the patients with some indications according to the pregnancy week are referred for the ultrasound examinations more than the other weeks, e.g. the patients in the first trimester for the double screening test or in the second trimester for anomaly screening are referred frequently, however, the number of patients for each week of gestation is tried to be at least 25.

Turan et al studied the reference ranges of DV in 902 velocity wave ratios of pregnant women, gathered retrospectively, obtained from two different fetal medicine centers, despite a standardized fashion, obtained by several sonographers and physicians. No data for the equipment of ultrasonography was given in this research (3). It is very well-known that ultrasonography is the most operator-dependent imaging modality. Our study includes the largest patient population in the medical literature and was performed prospectively using the same ultrasonographic equipment with the same preset adjustments in a single center by a single operator, a specialist (C.G.), who had been experienced in fetal imaging and certified by FMF. The measurements were estimated either in the classic, well-known spectral Doppler pattern of the ductus venosus or to the best of our knowledge, for the first time in the medical literature in the variants of the spectral Doppler waveforms, which were described recently (9). The wideband color Doppler technique (Advanced Dynamic Flow, Toshiba), differently other than previous studies, was used to visualize the slow flow fetal vessels without blooming artefact which was used to locate the DV and to place the sample gates. This technique provides to get faster spectral waveforms of the DV and more accurate and reproducible measurements.

**Conclusion**

In conclusion, with advancing technologies for the mapping of DV and the easier reproducible measurements, the limits of DV velocities were needed to be updated. The normal reference ranges for absolute flow velocities of S, v, D, a and Vm_Peak and indexes, which were derived from the velocities using the wideband Doppler technique in the largest patient population so far were studied prospectively in a single tertiary care center and can be used for the detection and follow up the fetal flow dynamics.

**Video 1.** The spectral Doppler waveform of ductus venosus blood flow at 12 weeks gestation
**Video 2.** The spectral Doppler waveform of ductus venosus blood flow at 34 weeks gestation in the oblique transverse plane
**Video 3.** The spectral Doppler waveform of ductus venosus blood flow at 34 weeks gestation of the same patients in figure 6 in the sagittal plane

**Conflict of Interest:** No conflict of interest is declared by the authors.
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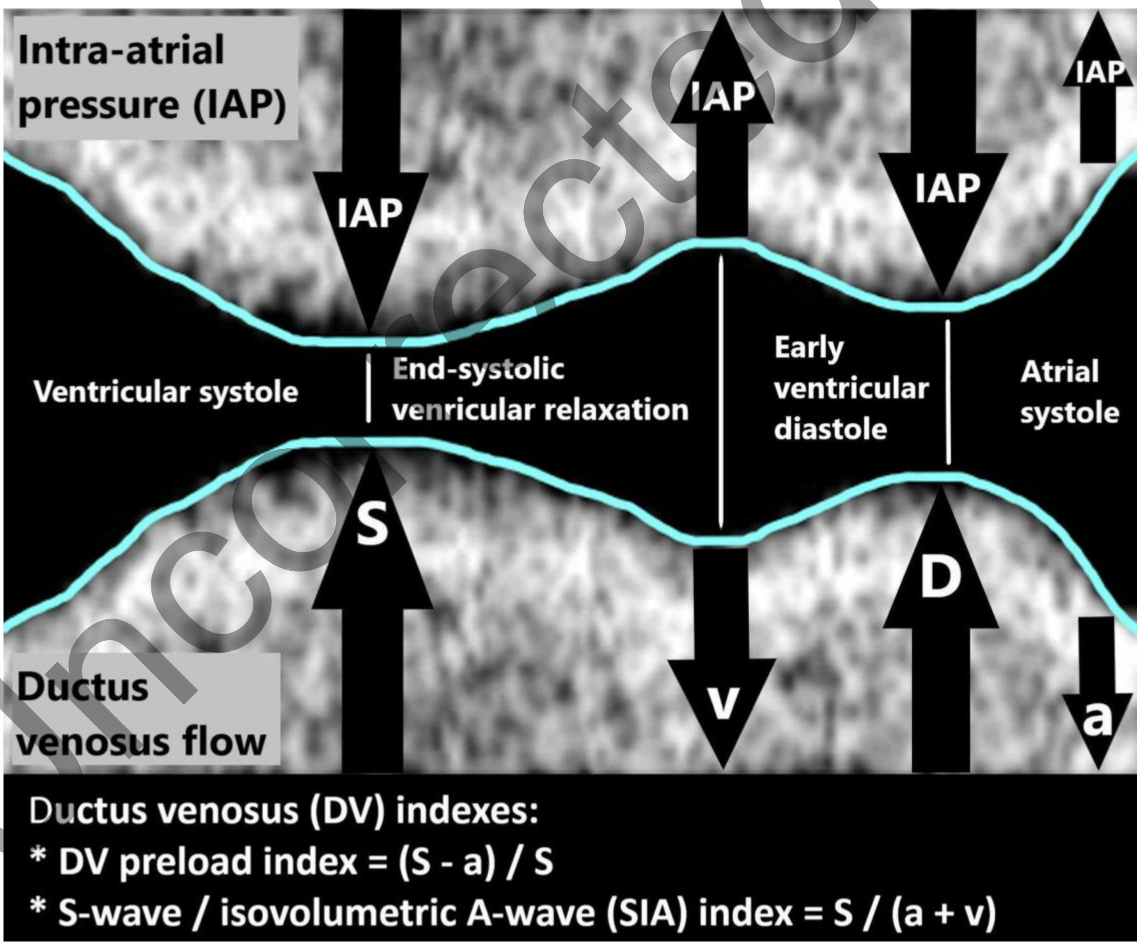


**Figure 1.** Relationships between the DV flow velocities and the intra-atrial pressure changes in a cardiac cycle. DV flow velocity increases while the intra-atrial pressure decreases and vice versa


**Figure 2.** The measurement of ductus venosus flow velocity and indices 12 weeks' gestation

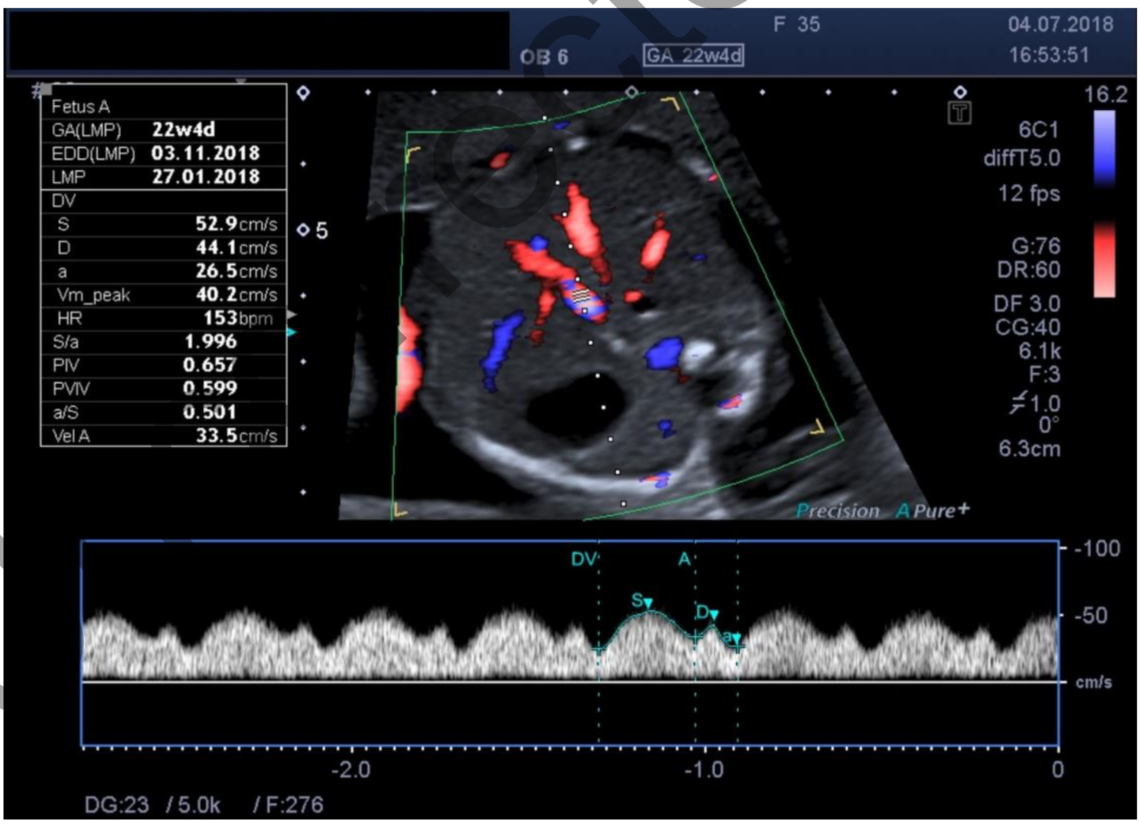


**Figure 3.** The measurement of ductus venosus flow velocity and indices 22 weeks' gestation in the oblique transverse plane

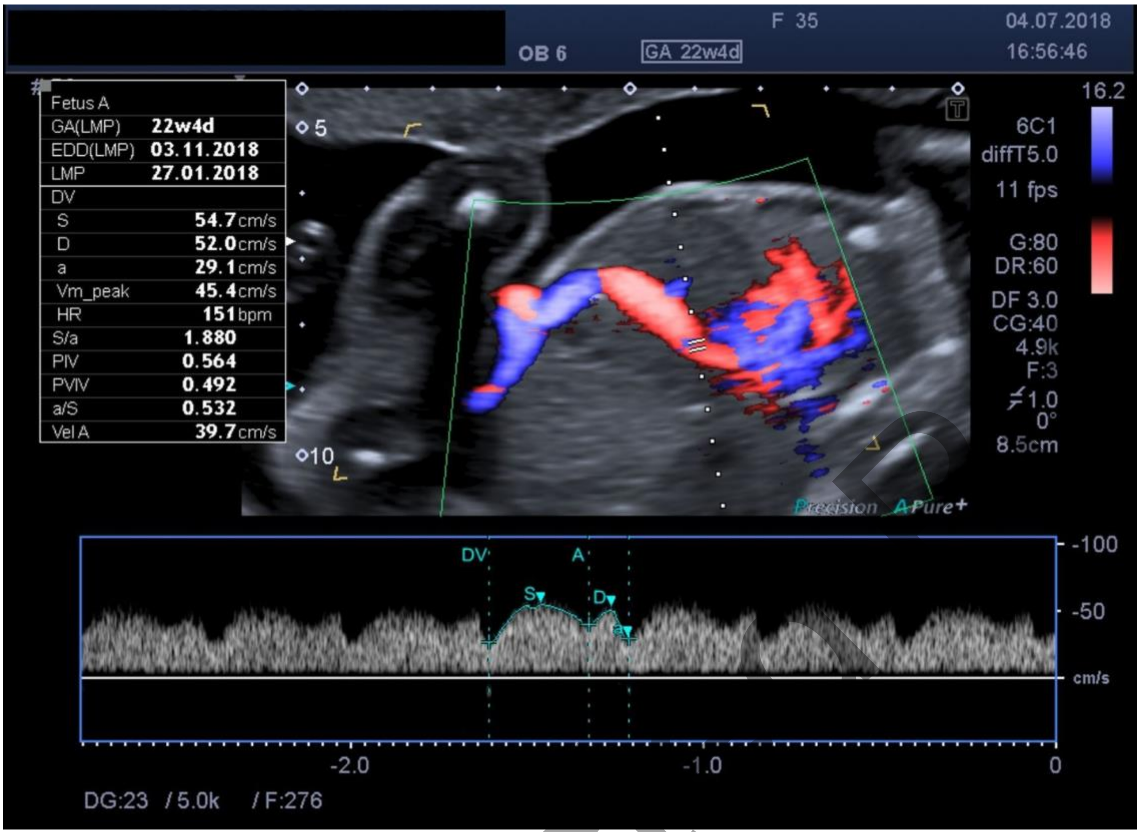


**Figure 4.** The measurement of ductus venosus flow velocity and indices 22 weeks' gestation of the same patients in figure 3 in the sagittal plane

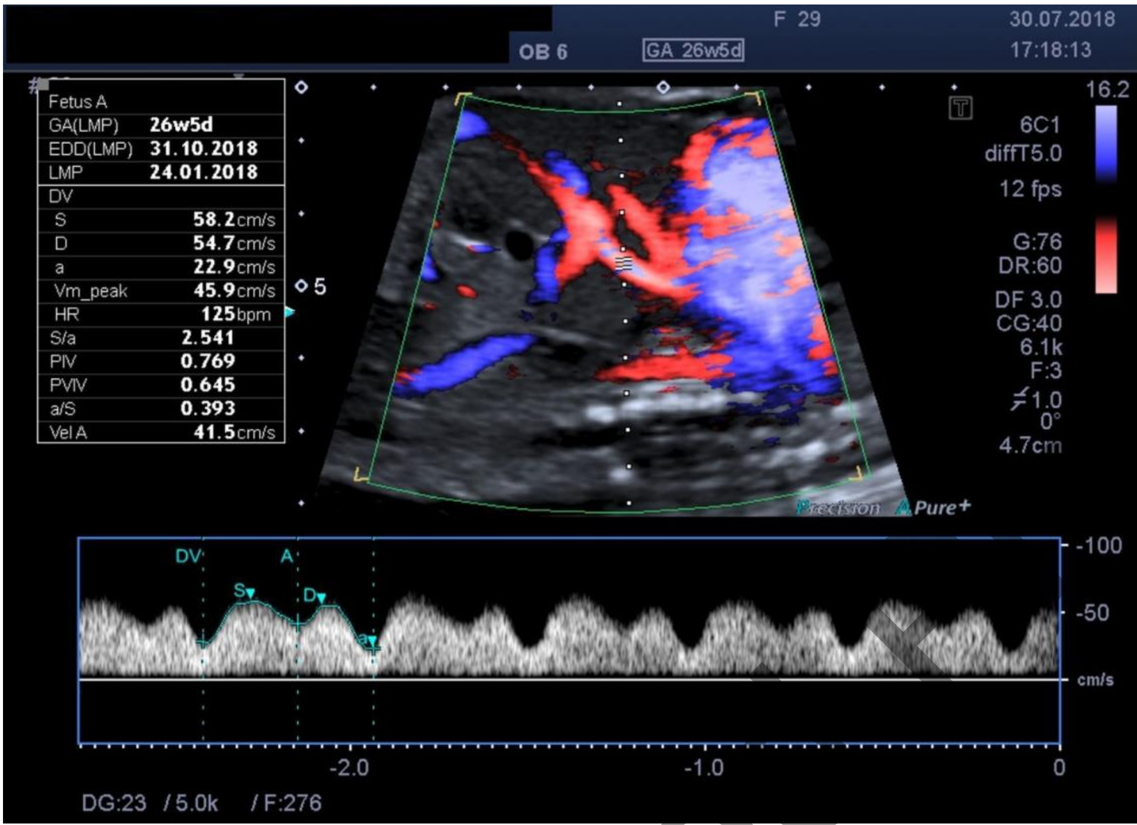


**Figure 5.** The measurement of ductus venosus flow velocity and indices 26 weeks' gestation


**Figure 6.** The measurement of ductus venosus flow velocity and indices 34 weeks' gestation in the oblique transverse plane

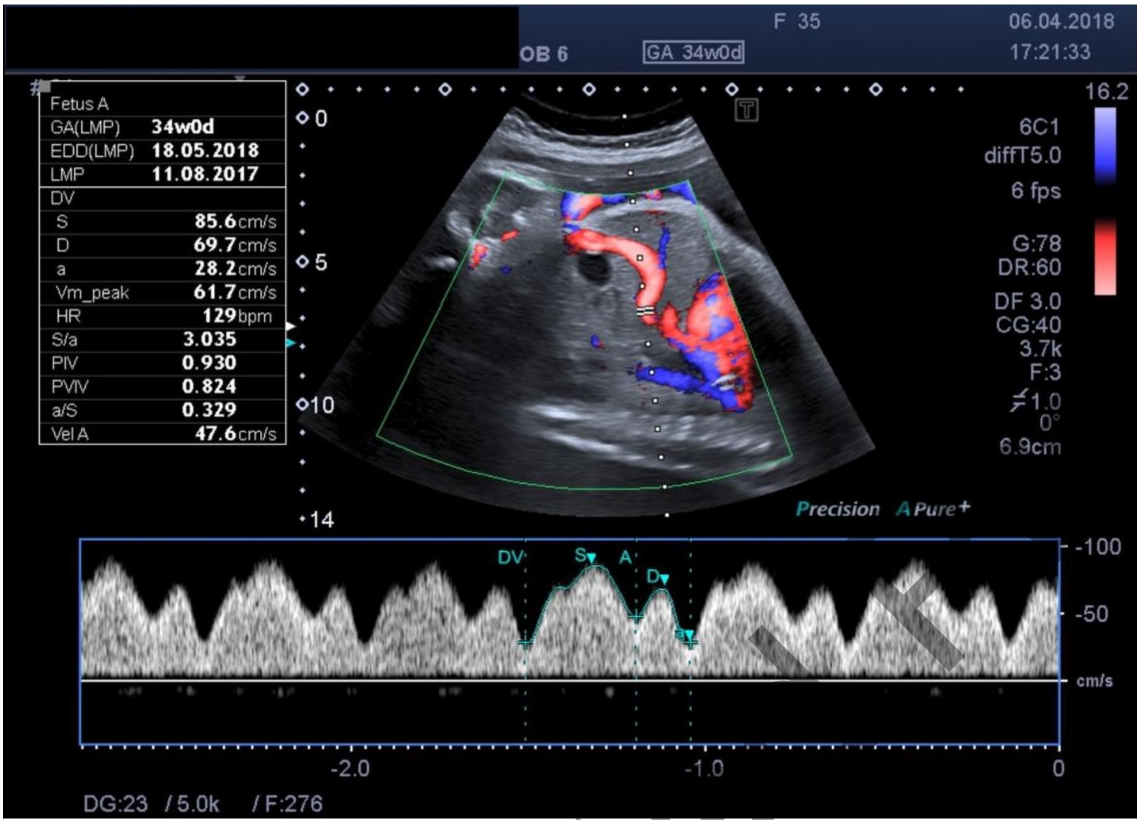


**Figure 7.** The measurement of ductus venosus flow velocity and indices 34 weeks' gestation of the same patients in figure 6 in the sagittal plane

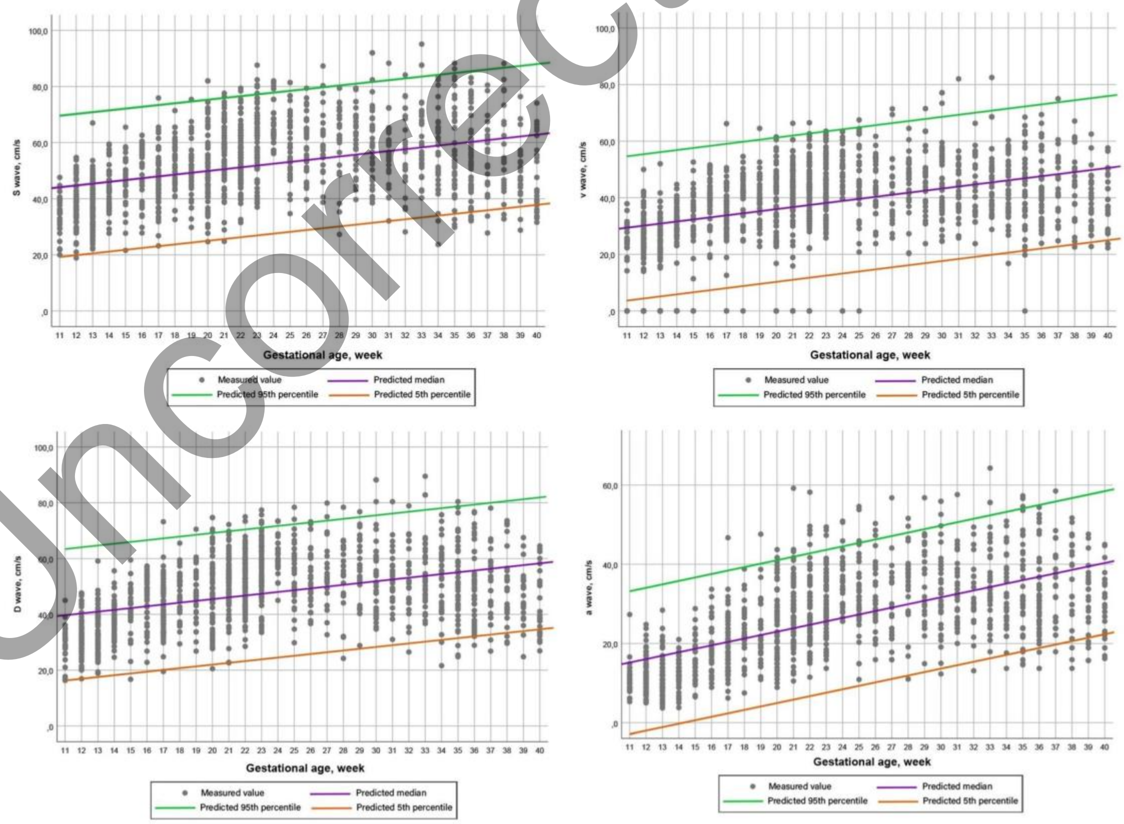


**Figure 8.** The scatter plots graphics for S, v, D, a wave (cm/s) against the gestational age

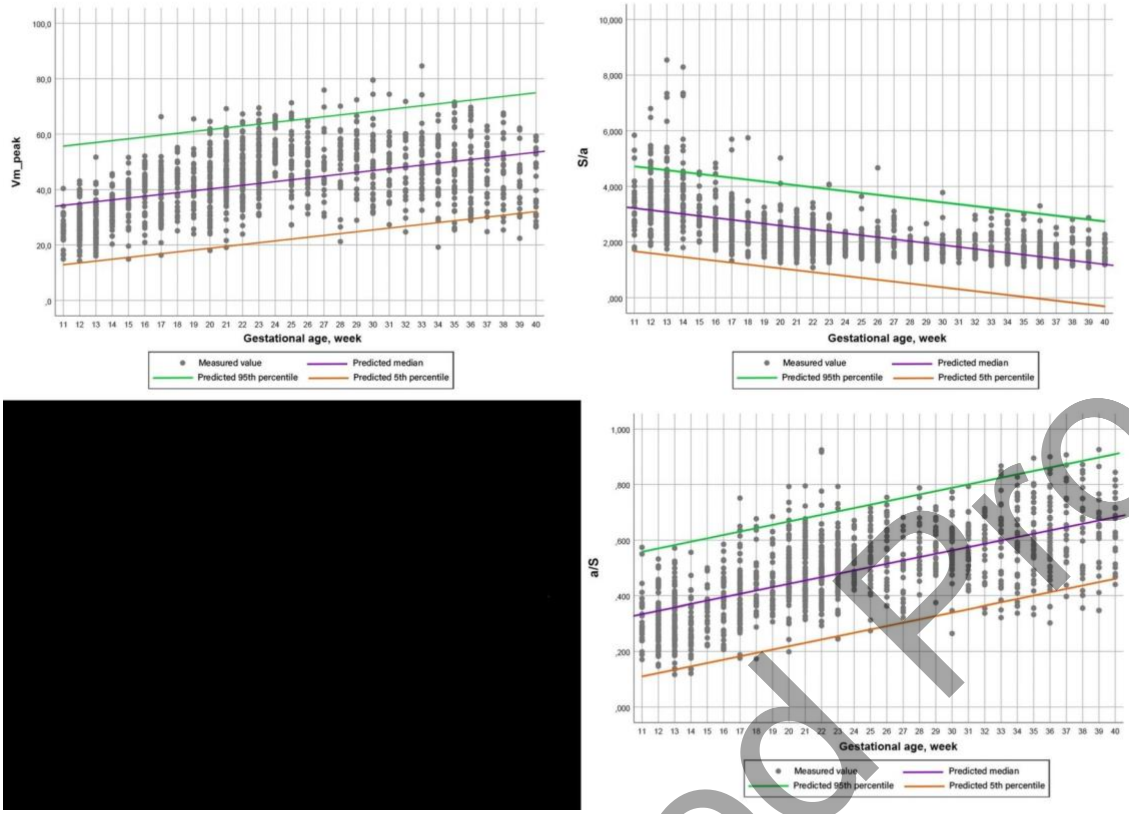


**Figure 9.** The scatter plots graphic for Vm_peak wave (cm/s), S/a and a/S ratios against the gestational age

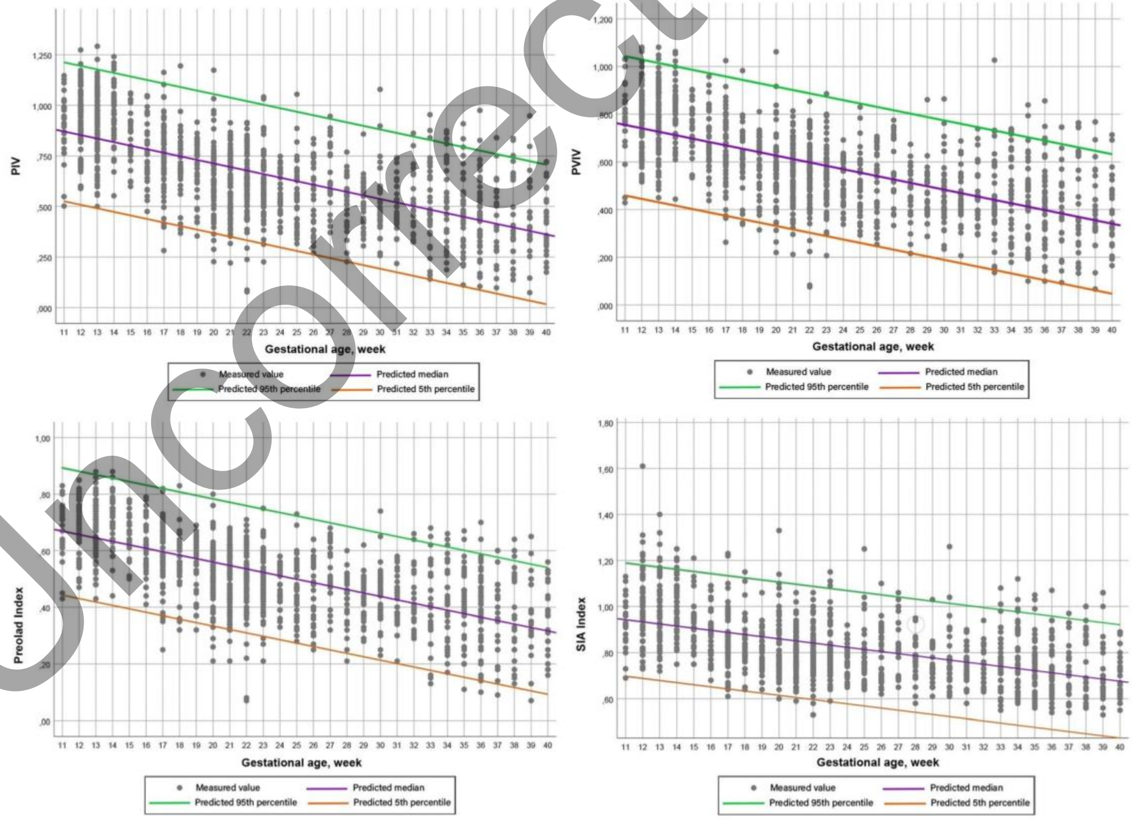


**Figure 10.** The scatter plots graphic for PIV, PVIV, preload and SIA indexes against the gestational age

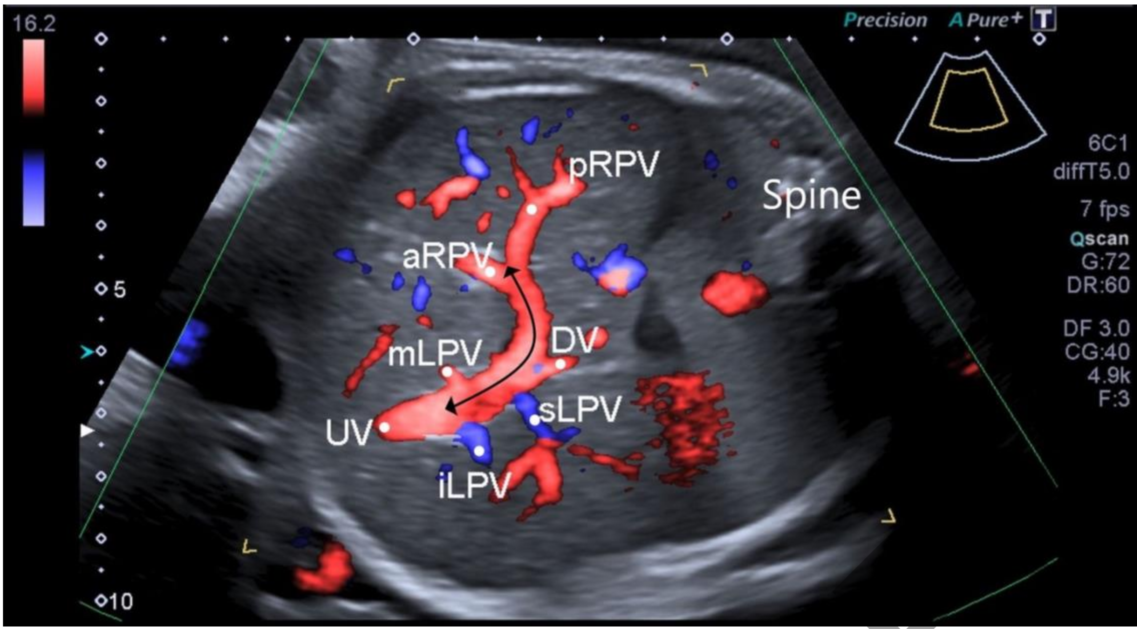


**Figure 11.** Afferent precordial venous system in an oblique axial color Doppler image. UV=Umbilical Vein, iLPV=Inferior branch of the left portal vein, sLPV=superior branch of the Left Portal Vein, DV=Ductus Venosus, Curved black line =Portal Sinus, mLPV= Medial branch of Left Portal Vein, aRPV=Anterior branch of the Right Portal Vein, pRPV=Posterior branch of the Right Portal Vein

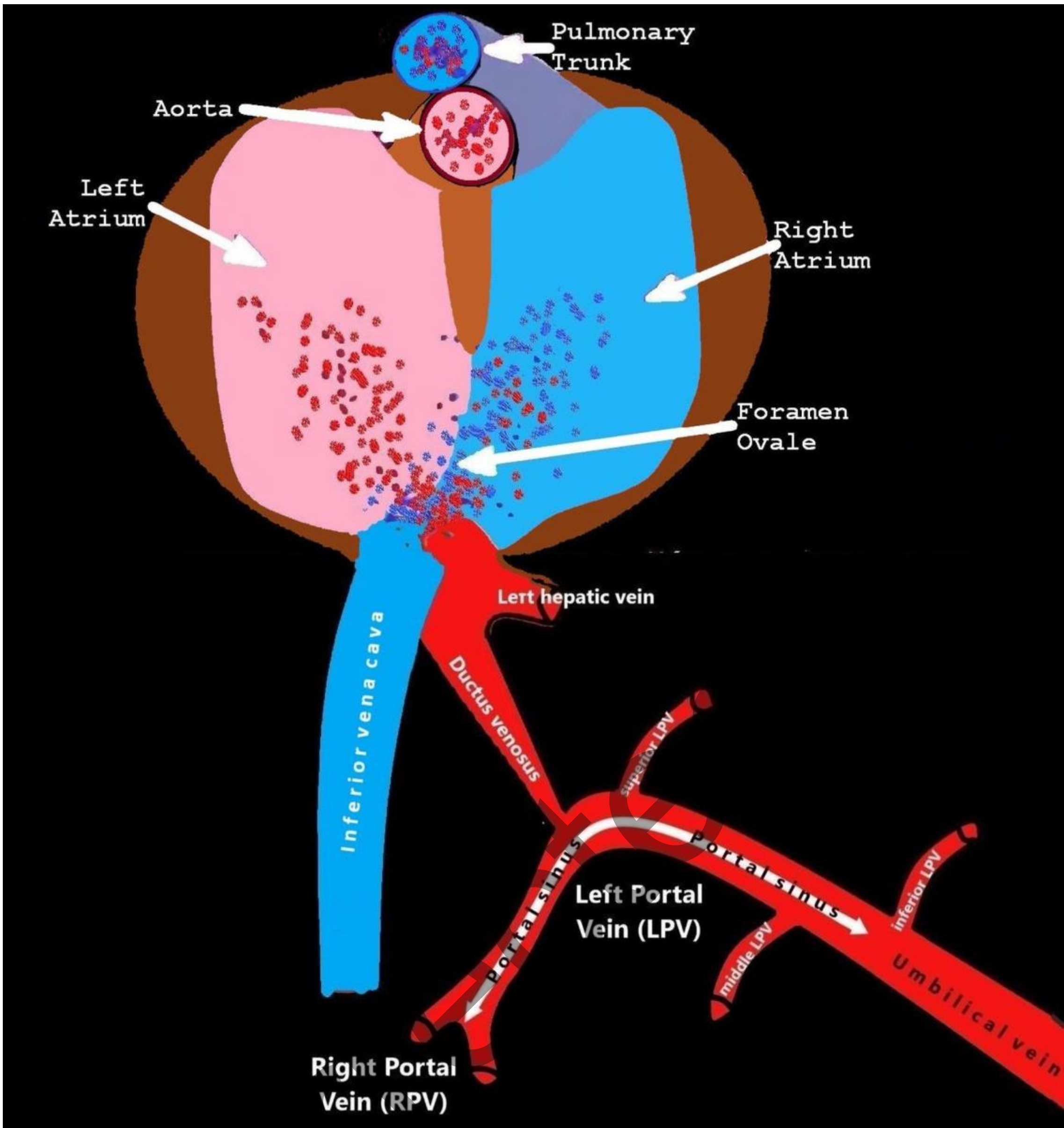


**Figure 12.** Flow distribution through the foramen ovale and the afferent precordial venous system in a painted illustration