Evaluation of Normal Fetal Ductus Venosus Using B-Flow Imaging with Spatiotemporal Image Correlation and Traditional Color Doppler Echocardiography

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Objective: To explore the feasibility of using four-dimensional echocardiography with B-flow and spatiotemporal image correlation (4DBF-STIC) imaging technology to detect fetal ductus venosus (DV), and establish the normal reference range for the ductus venosus diameter at 18–40 weeks gestation.

Methods: This was a prospective observational study to detect the DV in 354 normal fetuses at 18–40 weeks of gestation using color Doppler echocardiography (CDE) and 4DBF-STIC imaging. CDE was performed on an oblique transverse plane of the fetal abdomen, with scanning around the long-axis view of the aortic arch. The DV inlet was measured on a two-dimensional gray-scale image of the long-axis view of the DV. Offline analyses of all datasets were performed. Results: The inlet diameter of the DV increased with increasing gestational age. There were no gender-related differences in the DV diameter. Data revealed that 4DBF-STIC was the best method to detect the DV between 18 and 29 weeks of gestation. The visualization rate was higher when scanning around the long-axis view of the aortic arch with CDE than when scanning around the oblique transverse plane throughout the gestational period. Conclusions: Scanning around the long-axis view of the aortic arch using CDE was best suited for detecting the DV in clinical practice, whereas 4DBF-STIC was a feasible and promising technology to detect the fetal DV before 29 weeks of gestation. (Echocardiography 2015;32:325–331)

Key words: four-dimensional echocardiography, B-flow imaging, spatiotemporal image correlation, fetal, ductus venosus, color Doppler

The ductus venosus (DV) is an important fetal vascular structure as it connects the umbilical venous system to the inferior vena cava (IVC) near its insertion point into the right atrium.¹ It plays a key role in the fetal circulation because it diverts oxygenated blood from the placenta toward the right atrium, through the foramen ovale to the left heart, and thereafter to the brain.²⁻⁴ Agenesis of the ductus venosus (ADV) is an abnormality that represents abnormal anastomosis formation of the umbilical veins.⁵ This malformation is associated with major fetal anomalies, including cardiac abnormalities, chromosomal aberrations, hydrops, and adverse neonatal outcome.⁶⁻⁹ However, it is difficult to observe DV using two-dimensional (2D) gray-scale echocardiography because the inner diameter of the DV is very small. Color Doppler echocardiography (CDE) could provide more information, including identifying the direction of the blood flow. As such, it is easier to detect the DV using CDE rather than 2D gray-scale echocardiography.

B-flow is a novel method that uses ultrasound to detect blood flow, and allows the direct visualization of blood flow using gray-scale sonography.¹⁰ The most useful characteristics of B-flow are a wider bandwidth, higher frame rate, and higher spatial, temporal, and contrast resolution compared with CDE.¹¹ Because B-flow has no angle dependency, it provides easier image acquisition than color Doppler, regardless of the direction or angle of the blood vessels.

Spatiotemporal image correlation (STIC) is a four-dimensional (4D) ultrasound technology that allows dynamic multiplanar slicing and surface rendering of the fetal heart anatomy. Using reconstruction from the cine loop, it is possible to identify different cardiac planes and obtain considerable anatomic information.¹²⁻¹⁴ B-flow

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imaging sonography with STIC sweeps (4DBF-STIC) provides information regarding DV drainage that could be shown in a surface rendered cine loop.

The purpose of this study was to evaluate the clinical usefulness of 4DBF-STIC for visualizing normal fetal DV, and for measuring the DV inlet on the 2D gray-scale images to establish reference values for the fetal DV diameter. These reference values will enhance our understanding of venous return to the fetal heart in a normally developing pregnancy, and thus help us to identify hypoxemia.15

Methods:

Population:

This was a prospective study of 354 females with normal singleton pregnancies between 18 and 40 (mean 28) weeks gestation. The maternal age ranged from 22 to 34 (median, 28.5) years. The pregnant females were recruited between October 2011 and October 2012, and all were Asian. Routine prenatal screening was used to confirm that all the fetuses were in good health, without cardiac or extra-cardiac anomalies. All the pregnant females were without any maternal complications or high-risk factors (hypertension, diabetes, amniotic disorders, maternal medication) at the time of enrollment. Fetal age was determined based on the first day of the last menstrual period, and was confirmed using first-trimester and early second-trimester sonographic measurements. All subjects underwent postnatal echocardiography follow-up, with a minimum follow-up period of 6 months. Thirty-eight individuals were excluded: 25 for lack of follow-up, 5 because maternal complications were detected, 3 that were receiving maternal medication during pregnancy, 3 that delivered prematurely, and 2 with neonatal morbidity. The remaining 316 cases were divided into 6 subgroups according to the gestational weeks 18–21, 22–25, 26–29, 30–33, 34–37, and 38–40. All pregnant females underwent only one examination.

Ultrasonography:

A 4D ultrasound system (Voluson E8, GE Healthcare, Kretztechnik, Zipf, Austria) with a transabdominal probe (RAB 4–8 MHz) and STIC were used in this study. Fetal DV images were obtained, and the DV drainage into the right atrium was visualized using the following 3 methods.

Method 1: An oblique transverse plane of the fetal abdomen using CDE to identify the DV: A tracking scan of the umbilical vein in the oblique transverse plane of the fetal abdomen was performed. Because the ductus venosus has the highest blood flow velocity in the venous system, it is characterized by a highlighted area that is the portion immediately above the umbilical vein. Examination of the DV was performed during fetal quiescence, and the image was magnified so that the fetal thorax and abdomen occupied the whole screen (Fig. 1). All data were saved as movie clips for later analysis to determine whether the DV could be visualized.

Method 2: Scanning around the long-axis view of the aortic arch using CDE to identify the DV and measure the DV inlet on a 2D gray-scale image: First, the long-axis view of the aortic arch was shown and the probe was then moved slightly. A right ventral sagittal view of the fetal trunk was obtained and color flow mapping was then used to reveal the umbilical vein, DV, and fetal heart. This allowed the visualization of a highlighted area that was the portion immediately above the umbilical vein as well as the blood flow to the heart (Fig. 2). After the DV was displayed, “color off” was selected on the screen of the machine. The inner measurement of the DV was then determined in the isthmic portion near the junction with the umbilical vein. Using the memory function, the best frame was selected for an easier measurement of the inner diameter of the vein. The result was then recorded without the need to change the focus, allowing the examiner to perform the next measurement without delay. Participants who had <3 measurements of the vessel diameter were withdrawn from statistical analyses. All data were saved as movie clips for subsequent analysis.

Figure 1. Visualization of the fetal ductus venosus in the oblique transverse plane of the abdomen of a 28-week fetus using color Doppler echocardiography. It is characterized by a highlighted area, which is the portion immediately above the umbilical vein. DV = ductus venosus; ST = stomach; UV = umbilical vein.
Method 3: The use of 4DBF-STIC to identify the DV: Volume datasets were acquired using sagittal sweeps through the fetal thorax. The automated sagittal sweeps began at the long-axis view of the aortic arch. After demonstrating blood flow using 2D B-flow, B-flow STIC images were obtained using a single automatic volume sweep scan. The regions of interest included the atrial chambers, great arteries, and veins returning to the fetal heart. The B-flow settings were as follows: sensitivity, 6; dynamic range, 9; and persistence, 2. The STIC collecting angle (angle of the sweep) ranged from 25 to 40°, and the acquisition time ranged from 12.5 to 15 sec. The sweep angle and the acquisition time increased with gestational age. Whenever possible, acquisition was performed in the absence of fetal movement. Patients were asked to breathe slowly and evenly. The STIC volumes were reconstructed immediately, and displayed in a cine loop once an adequate acquisition has been achieved. The volume datasets were stored on the hard disk of the computer for later offline analysis. The examinations were exported to a USB disk and transferred to a personal computer for evaluation using specialized software (4D Viewer, version 7.0; GE Medical Systems, Kretztechnik, Zipf, Austria).

All volume datasets were presented using the multplanar modality. A combination of smooth surface and gradient light algorithms was adopted with surface rendering. First, the long-axis view of the aortic arch was displayed in Figure 3A. The image was adjusted and rotated along the X, Y, and Z axes, and the DV to the heart was displayed in the rendered image in Figure 3D. The size of the sampling box in Figure 3B was decreased to clearly visualize the DV in the rendered image in Figure 3D. Postprocessing adjustments were used to improve the image quality (Fig. 3, movie clip S1).

Two experienced prenatal screening sonographers (Z.Y. and W.X.G.) performed the fetal echocardiography with CDE, volume data acquisition, postprocessing, and analysis together. Inter-observer variability for 4DBF-STIC was resolved by having another experienced sonographer (C.A.L.) reprocess and reanalyze the 4D volumes in 48 randomly selected fetuses according to gestational age (8 fetuses for each 18–21, 22–25, 26–29, 30–33, 34–37, and 38–40 gestational weeks) 15 days later. The inlet diameter of the DV was recorded for each fetus and the mean of multiple measurements was used.

Statistical analysis:
The statistical package SPSS 17.0 (SPSS, Chicago, IL, USA) was used for statistical analyses. The diameters of male and female fetuses are presented as means ± SE. Independent sample t-tests were used to assess differences between male and female fetuses. The relationships between the inlet diameter of the DV and gestational age were analyzed using Pearson’s correlation analysis. P < 0.05 was considered statistically significant.

Results:
The DV was detected in 276 fetuses and the DV inlet diameter was obtained from 216 fetuses. The distribution of the participants is shown in Figure 4. The DV inlet diameters exhibited a gestational age-dependent increase (r = 0.703 and P < 0.001, Pearson’s correlation analysis, Fig. 5). There were no gender-related differences in DV diameter between 18 and 40 gestational weeks (P > 0.05, t-test, Table 1).
The mean scanning times for an oblique transverse plane of the fetal abdomen with CDE, scanning around the long-axis view of the aortic arch, and 4DBF-STIC were 1.0 ± 0.2, 2.9 ± 0.4, and 8.5 ± 3.8 min, respectively. The mean time for 4D volume postprocessing and analysis was 10.5 ± 3.6 min. It took much more time to detect DV using 4DBF-STIC than the other 2 methods.

The visualization rate of the DV obtained using an oblique transverse plane of the fetal abdomen with CDE, scanning around the long-axis view of the aortic arch, and 4DBF-STIC are presented in Figure 6. When patients were grouped according to gestational age, 4DBF-STIC was the best method to detect the DV between 18 and 29 weeks of gestation. Scanning around the long-axis view of the aortic arch with CDE detected more of the DV than an oblique transverse plane of the fetal abdomen with CDE throughout the gestational period.

**Discussion:**

The early detection of ADV is important in perinatal care. When it is diagnosed, affected fetuses require detailed assessment as they are at increased risk of other congenital anomalies. In fetuses with ADV, there are 2 different routes for umbilical venous return: extrahepatic umbilical venous drainage bypassing the liver and intrahepatic umbilical venous drainage without liver bypass.\(^5,6\) The classification of ADV into extra- and intrahepatic umbilical vein insertion groups has an important impact on prognosis. Our study described several DV detection methods that could be used during prenatal screening, and might provide some information to help improve current screening methods.

Two-dimensional gray-scale echocardiography is not an effective method to detect the DV. However, when visualizing the shunt diameter, 2D gray-scale ultrasound represented the true dimensions more reliably. Therefore, we measured the inlet diameter of the DV using 2D gray-scale ultrasound. To increase the display rate of the 2D gray-scale ultrasound, color Doppler was used to

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**Figure 4.** Description of the study population.

**Figure 5.** Relationship between the fetal ductus venosus inlet diameter and gestational age, as measured using two-dimensional gray-scale imaging (n = 216). Each plot is the mean of 4 consecutive measurements. Ductus venosus inlet diameters (P < 0.001 \( r = 0.703 \)) had a highly positive linear correlation with gestational age. The line of “---” represent the 5th and 95th percentiles.
determine the DV, and then selected “color off” on the screen of the machine after the DV was displayed. The 2D gray-scale images of the DV were then obtained. This is the first time that this method has been used to measure the DV. Previous reports evaluated the DV of fetuses using color and pulsed Doppler during the second trimester, and also measured the peak velocity.\textsuperscript{16,17} Doppler examination of the DV has increased importance in fetal evaluation and in the management of fetuses with intrauterine growth restriction (IUGR).\textsuperscript{18} For example, a marker of fetal acidosis and an increased risk of perinatal death is an increased DV blood velocity.\textsuperscript{19} A previous study reported an increase in the velocity and decrease in the pulsatility index of the DV at all gestational ages.\textsuperscript{20} Fetuses with congenital heart disease had a larger than normal DV size, and an abnormal DV pulsatility index.\textsuperscript{21}

This study provided a normal reference range of the DV diameter at 18–40 weeks gestation. These reference values will improve our understanding of venous return to the fetal heart in a normally developing pregnancy. The results demonstrated that the inlet diameter was age dependent. In this way, we hypothesize that the diameter of the DV could be a parameter for fetal evaluation in certain conditions such as acidosis and IUGR, particularly when Doppler examination of the DV cannot be achieved. Therefore, additional studies assessing its validity and reliability in fetal pathological conditions should be performed.

Color Doppler is indispensable for sonographic evaluation of the anomalous shunt. An oblique transverse plane of the fetal abdomen combined with color velocity maps was used to visualize DV. This was an effective way of excluding ADV

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Results of Measurements of the DV Inlet in Male and Female Fetuses</th>
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<tbody>
<tr>
<td>Gestational Age Weeks</td>
<td>Inlet Diameter of the DV (mm)</td>
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<tr>
<td>-----------------</td>
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<tr>
<td>18–21</td>
<td>18 (1.23 ± 0.04)</td>
</tr>
<tr>
<td>22–25</td>
<td>32 (1.53 ± 0.05)</td>
</tr>
<tr>
<td>26–29</td>
<td>38 (1.76 ± 0.05)</td>
</tr>
<tr>
<td>30–33</td>
<td>14 (1.83 ± 0.05)</td>
</tr>
<tr>
<td>34–37</td>
<td>11 (2.00 ± 0.08)</td>
</tr>
<tr>
<td>38–40</td>
<td>8 (2.21 ± 0.10)</td>
</tr>
<tr>
<td>38–40</td>
<td>121 (1.68 ± 0.03)</td>
</tr>
</tbody>
</table>

n = number of measurements of DV diameters ≥3 at that gestational age.

Figure 6. The visualization rate of the DV in 6 subgroups according to gestational weeks 18–21, 22–25, 26–29, 30–33, 34–37, and 38–40 using an oblique transverse plane of the fetal abdomen with CDE ( ), scanning around the long-axis view of the aortic arch with CDE ( ), and 4DBF-STIC ( ).
during prenatal screening, because it was simple and rapid.

Scanning around the long-axis view of the aortic arch had a higher detection rate in our study in fetuses 18–40 weeks of gestation than the oblique transverse plane. There are 2 possible reasons for this. When the fetal spine is up, it is easier to obtain DV scanning around the long-axis view of the aortic arch than an oblique transverse plane. Scanning around the long-axis view of the aortic arch enabled us to avoid contamination from the intrahepatic portion of the umbilical vein, the left hepatic vein, and the IVC. This was a good method because it performed consistently well, enabling the examiner to identify the DV in ~90% of fetuses.

Unfortunately, color Doppler was too prone to “bleeding” the color beyond the vessel to be suitable for providing accurate measurements. Research has demonstrated that infants with a shunt diameter that was equal to or larger than the umbilical vein diameter had a significantly poorer outcome than those with a narrower shunt. It was important to regulate the technical settings in CDE to optimize the sonographic images. A low-velocity scale or pulse repetition frequency allowed better visualization of the vessel. However, it was sometimes appropriate to increase the scale to reduce blood spill.

Four-dimensional ultrasound and STIC provide an additional method to identify the DV. These techniques offer an easy to use feature for acquiring data from the fetal heart and visualizing it in a 4D cine sequence. B-flow is a unique technique to enhance signals from weak blood reflectors from vessels and, at the same time, suppress strong signals from the surrounding tissues. B-flow imaging is a non-Doppler technology that is angle independent, and permits relatively high frame rates with excellent spatial resolution. Blood flow in the vessels is realistically represented and more clearly delineated on B-flow than on color Doppler imaging. The combination of both techniques has proved to be promising for visualizing the low-velocity vessels and the great arteries. Our findings confirmed this application for detecting DV.

Four-dimensional ultrasound and STIC provide a 3D reconstruction of blood vessels, and allows real-time visualization of complex anatomical details of, or size differences among, the great vessels and connecting caval veins. BF-STIC showed both the shape and contour of the vein in its entirety. This helps us improve our understanding of the course of the umbilical vein, demonstrating the validity of the 3D tool.

In our study, 4DBF-STIC had a higher detection rate for the DV than the other 2 methods at 18–29 gestational weeks. This method made it possible to visualize the normal intrahepatic umbilical vein, the DV, the inferior vena, and the entire course of blood vessels simultaneously. Knowledge of these anatomical relationships is paramount for diagnosing ADV. The main advantages of examining the DV using BF-STIC compared with 2D are that it allows the display of virtual planes that cannot be visualized directly in 2D ultrasound by rotating planes through 180° along the 3 rotational axes. The DV can also be observed at any angle. Four-dimensional STIC is a unique technique for fetal heart screening that can obtain the storage volumes of cardiac anomalies, or of the normal heart, for reviewing findings and/or remote consultations.

Nevertheless, the quality of a STIC acquisition contains some technical limitations. It can be modified negatively by fetal body movement, breathing movements, hiccups, and changes in heart rate. In addition, the low detection ratio of DV during late gestation (30–40 weeks) could have been caused by increased acoustic shadows of the fetal ribs. A fetal position with the spine up also produces some acquisition problems, since acquisition is the easiest when the spine of the fetus is not in the ventral position. A prerequisite for a good volume is the optimal presetting of the B-flow during the 2D scan before acquisition. With 2D imaging, the operator must reconstruct a series of planar images to represent the 3D anatomy. The time taken for volume data acquisition and postprocessing was longer than scanning around the long-axis view of the aortic arch (19 vs. 2 min). In contrast, when scanning around the long-axis view of the aortic arch with CDE, it was easier to detect the DV because the probe can be moved and adjust the angle of the beam to avoid interference from the acoustic shadowing.

The limitations of this study include the lack of a subgroup of fetuses with anomalous DV returns to verify the accuracy of the findings. It is difficult to collect a sufficient number of abnormal fetuses because ADV is a very rare cardiac condition. In addition, the reproducibility and validity of the 4D methodology requires additional evaluation. Moreover, data acquisition and postprocessing of the 4D volumes require increased sonographer experience and expertise, which restrict the application of the 4D method. Finally, a certain level of training is needed before these methods are introduced into clinical practice.

Conclusions:
Scanning around the long-axis view of the aortic arch using the CDE proved to be the most suitable method for detecting the DV in clinical practice. Four-dimensional BF-STIC was superior for detecting the DV before 29 gestational weeks.
The 4DBF-STIC method should be considered complementary to traditional CDE, because it helps to understand the anatomy and the spatial relationships of the fetal abdominal blood vessels.

References

Supporting Information
Additional Supporting Information may be found in the online version of this article:

Movie clip S1. For Figure 3.