Cardiac Doppler flow velocities in human fetuses

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ABSTRACT Cardiac Doppler flow velocity studies were performed in normal human fetuses between 18 and 40 weeks of gestation. Two-dimensional linear array and sector scanning techniques were used for the initial evaluation of the fetuses, which included a standard ultrasound examination to determine normal anatomy and estimated gestational age and weight. Fetal cardiac ultrasound examination was then performed, with four-chamber, short-axis/great vessel, long-axis/left ventricular outflow tract, and aortic arch views obtained. Pulsed echo Doppler instrumentation was used to obtain flow velocity measurements through the tricuspid, pulmonary outflow, mitral, and aortic outflow regions. Calculation of transvalve volume flow for mitral and tricuspid valves was performed by combining the valve annulus sizes and calculated mean temporal velocities for the valves. Maximal flow velocities were greater through the tricuspid (mean maximal velocity 51 ± 1.2 [SE] cm/sec) than through the mitral (47 ± 1.1 cm/sec; p < .05) valve regions, with a wide range of scatter for results between fetuses but less than 6% average variation in the individual fetuses during gestation. For 18 fetuses, right heart dimensions and volume flows (mean 307 ± 30 ml/kg/min) were greater than left heart dimensions and volume flows (232 ± 25 ml/kg/min). Doppler echocardiography may prove to be useful as an adjunct to imaging echocardiography for evaluation of fetal cardiac anatomy and function. 


THE HUMAN FETAL HEART can now be examined by ultrasound and echocardiographic techniques.1-8 This allows fetal cardiac anatomy and physiology to be studied in an obstetric population for the purpose of prenatal diagnosis and management.

Doppler echocardiographic techniques can be used to determine flow velocity, and in conjunction with two-dimensional real-time imaging, can provide estimates of volume flows.9-11 These techniques were used in 90 examinations of 75 fetuses to establish normal values of temporal flow velocity and to attempt to assess transvalve volume flows in the human fetus.

Methods

Patients were selected from the Obstetrics Clinic at the Arizona Health Sciences Center and from outside referrals. Human Subjects Committee approval was obtained for the study, and informed consent was obtained from each participating mother before the examination. Fetuses were examined between 18 and 40 weeks gestation; all fetuses have been examined postnatally and have had normal cardiac findings.

The instruments used included an Aloka 256 element linear array scanner and a 3.5 or 5 MHz Honeywell Echo Doppler scanner. With either scanning frequency, Doppler interrogation was performed at 3.5 MHz. Pulse repetition frequency for Doppler was 9500 at 6 to 12 cm depth of investigation so that the maximum unambiguously detectable velocity was 85 cm/sec when sampled parallel to flow.

Routine ultrasound scan measurements of each fetus included biparietal diameters, abdominal diameters, femur lengths, amniotic fluid volume, and placental location. Fetal weight was calculated on the basis of ultrasound measurements.12

Cardiac views attempted included four-chamber, four-chamber/left ventricular outflow, short-axis/pulmonary arterial, and aortic arch imaging.

Examination technique. Doppler velocity measurements were obtained by placing the Doppler sample volume immediately distal to the valve leaflets in the ventricle or great vessel into which the blood was flowing. Sample volume length was between 0.1 and 0.3 cm for these studies. The location of the pulsed Doppler gate was verified by two-dimensional ultrasound both before and after each Doppler tracing was obtained. The direction of blood flow was estimated to be perpendicular to the plane of the valve anulus within the plane of imaging. The angle between the estimated direction of blood flow and the Doppler beam was set and the angle indicated directly by the instrument. During Doppler flow velocity recordings, fine angulation of the transducer was performed until the highest maximal velocity tracing pattern possible was obtained at each location studied. In 10 studies, fetuses were examined sequentially by two examiners (S. S. and K. L. R.). Estimates of the angle between the Doppler beam and the direction of blood flow

Vol. 73, No. 1, January 1986
varied less than 10 degrees between examiners. Peak velocities obtained by the individual examiners varied with fetal respiration and fetal movement. The measurements were used only when a series of 3 consecutive beats with the highest velocity and of similar appearance was obtained in the absence of fetal breathing and movement.

**Measurement of records.** Maximal and mean temporal velocities were determined from page print outputs of the gray scale Doppler spectrum by means of a minicomputer. Maximal velocities were measured to the highest modal velocity (the darkest portion of the spectrum) in either systole or diastole. Temporal mean velocities were calculated by planimetering the area underneath the gray scale spectral velocity display throughout the cardiac cycle and by dividing by the time over which the flow was traced. Flow velocities were traced along the zero line during no-flow periods, diastole for the great arteries and systole for the atrioventricular valves. An average of 3 beats was used to determine the values reported. Measured velocities were angle-corrected by dividing by the cosine of the angle of incidence. Mean flow velocities were not corrected for heart rate. The normal fetus has a heart rate between 120 and 160 beats/min, and no fetuses in this study had abnormal heart rates. Maximal velocity tracings could be obtained with a variation of less than 10% by the individual examiners and had similar reproducibility when sequential studies by the two examiners were compared. Repeated tracings of the same printed outputs by the individual examiner varied less than 3 cm/sec for maximal velocity and less than 0.5 cm/sec for temporal mean velocity calculations, and similar variation was found between examiners. All measurements were performed by two examiners (S. S. and K. L. R.).

**Volume flow estimates.** We attempted to estimate volume flow across the atrioventricular valves in a subset of fetuses \( n = 18 \) of 26 attempts) studied between 26 and 30 weeks of gestation. To obtain volume flow measurements across the atrioventricular valves, linear array four-chamber views were obtained and mitral and tricuspid valve anulus diameters were measured in the axial direction. Doppler flow velocities were then obtained after changing fetal position so that flow was consistently toward or away from the transducer through the atrioventricular valves and sampling could be obtained at an angle of less than 30 degrees. Transvalvular flows were calculated with the formula:

\[
Q = \frac{\text{mean } V \times A}{\cos \theta}
\]

where \( Q \) = flow, mean \( V \) = mean temporal velocity, \( A \) = area, and \( \theta \) is the angle of incidence. For the purposes of these calculations, tricuspid and mitral valve anulus diameters in four-chamber views were considered to represent the diameters of circular flow orifice areas in early diastole. This dimensional measurement was undertaken immediately before or after the Doppler measurements. The time in the cardiac cycle during which flow area was estimated was determined by slow motion videotape playback from two-dimensional ultrasound studies. Measurement of the two-dimensional images was performed from endocardial wall to endocardial wall at the valve anulus just after the opening of the atrioventricular valves. Because of the small size of the structures examined (diameters of 0.44 to 1.2 cm), variations in orifice size across the atrioventricular valves during diastole were difficult to appreciate on video playback, and therefore the maximum diameter obtained on the frame just after atrioventricular valve opening was selected. Valve flow area was calculated by multiplying \( (\text{diameter}/2)^2 \) by \( \pi \). All diameters were measured and areas calculated by one examiner (S. S.). Annular diameter measurements varied less than 1 mm for either valve with repeated measurements.

Student’s t test for unpaired values was used to compare maximal and mean temporal flow velocity measurements. Results are reported as mean \( \pm \) SE.

**Results**

Ninety examinations were performed in 75 fetuses. Thirteen fetuses were studied serially. Figure 1 shows a representative four-chamber view of the fetal heart and typical tricuspid and mitral valve tracings obtained.
in these views. A short-axis/pulmonary arterial view with a pulmonary arterial flow velocity tracing is shown in figure 2. Figure 3 demonstrates a typical left ventricular outflow tract view along with an aortic valve region velocity tracing. As can be seen from the data in figures 4 and 5, we had greater than 60% success rate for recording atrioventricular valve velocities and pulmonary arterial velocities, and less than 50% success for the aortic recordings if we set criteria that flow must be recorded at less than a 30 degree angle of incidence. A wide scatter was noted in velocities for the whole series, although serial examinations in individual fetuses showed less than a 6% averaged variation for the group in maximal velocities across atrioventricular valves throughout gestation in individual fetuses (table 1).

For the entire group, average maximal and mean temporal velocity in the tricuspid valve region were 51 ± 1.2 (SE) cm/sec (range 34.1 to 78.2) and 11.8 ± 0.4 cm/sec (range 7.2 to 16.9), respectively (figure 4). This was greater than the maximal (47 ± 1.1 cm/sec, range 20.8 to 67.6; p < .05) and not different from the mean (11.2 ± 0.3 cm/sec, range 6.6 to 16.5; p > .05) temporal flow velocity through the mitral valve. In 43 fetuses in whom both tricuspid and mitral valve velocity measurements were performed at the same gestational age, tricuspid valve maximal velocity exceeded mitral valve maximal velocity in 73% and tricuspid valve mean velocity exceeded mitral valve mean velocity in 68%.

The maximal velocity through the pulmonary arterial region for the group as a whole was 60 ± 1.9 cm/sec (range 42.1 to 81.6); mean temporal velocity was 16 ± 0.6 cm/sec (range 9.2 to 25.7). Compared with the pulmonary arterial flow velocities, the flow across the aortic valve region showed a maximal velocity of 70 ± 2.6 cm/sec (range 56.0 to 94.0; p < .01) and a mean temporal velocity of 18 ± 0.7 cm/sec (range 13.7 to 22.5; p < .01) (figure 5), but there was more scatter and more angle correction used in the aortic data and fewer fetuses were successfully studied for aortic flow. In 22 fetuses in whom both pulmonary arterial and aortic valve region maximal and mean velocities were
measured at the same examination, aortic measurements exceeded pulmonary arterial measurements in 68% for both phasic maximal and temporal mean determinations.

For atroioventricular valves, late diastolic velocities coinciding with atrial contraction were consistently higher than early diastolic filling velocities, resulting in an A-wave dominant Doppler tracing in 97% of the fetuses examined (figure 1). This differs from the pattern seen in older children and adults, in whom the early diastolic Doppler flow velocity peak is dominant.

Eighteen fetuses were examined between 26 and 30 weeks gestation for the purposes of estimating mitral and tricuspid volume flows. This is a time of accelerating growth in the fetus. Criteria for inclusion were axial measurements of atroioventricular valve anuli (figure 6) and then rotation to allow velocity interrogation for both valves at an angle of less than 30 degrees during the same examination. Dimensional measurements for atroioventricular valve rings showed wide scatter as a function of estimated fetal weight, as of course did calculated volume flows. For the 18 fetuses in this part of the study, area measurements for atroioventricular valves ranged from 0.26 to 0.74 cm² for the tricuspid valve and 0.25 to 0.62 cm² for the mitral valve. Tricuspid anulus measurements were consistently larger than mitral valve measurements, and tricuspid flow volumes (307 ± 30 ml/kg estimated fetal weight/min) were statistically larger than mitral flow volumes (232 ± 25 ml/kg estimated fetal weight/min; p < .01) (figure 6). There was wide scatter in the data, but in 15 of 18 fetuses the tricuspid flow/mitral flow volume ratio was greater than 1 (range 0.89 to 1.81), and for the group the ratio was 1.3:1.

**Discussion**

Fetal cardiac blood flow patterns differ from those in the neonate and the adult. Flow in the fetus results from simultaneous ejection from both right and left ventricles into the systemic circulation. Vena cava inflow in the fetus is split to either the left atrium through the patent foramen ovale and eventually into the ascending aorta, or to the tricuspid valve, into the right ventricle, and pulmonary artery, with most of the flow continuing across the ductus arteriosus into the descending aorta. Fetal cardiac function has been studied

[FIGURE 4. Angle-corrected maximal and mean temporal flow velocities (group means ± SE) are shown for the fetal tricuspid and mitral valves. Max = maximal.]

[FIGURE 5. Angle-corrected maximal and mean temporal flow velocities (Group mean ± SE) are shown for the fetal pulmonary artery and aorta. Max = maximal.]
in the lamb, but the invasive nature of the methods used precludes studies in the human fetus.

In our study, peak Doppler filling velocities across the tricuspid valve were higher than those across the mitral valve, and valve volume flow across the tricuspid valve was greater, consistent with the right heart dominance previously demonstrated in normal fetal animals studied by Rudolph and Heymann.13 It would be expected that pulmonary arterial volume flow would be greater than aortic flow, and in our previous study of normal fetuses, the pulmonary arterial (PA) diameter slightly exceeded the aortic (AO) diameter (PA/AO: 1.2/1).2 Despite increased preload volume to the right ventricle compared with the left, aortic peak velocity exceeded pulmonary arterial velocity. This may reflect a better mechanical performance of the left ventricle or a difference in afterload prenatally even though left ventricular stroke volume is less than right ventricular flow volume. There was, however, wide scatter and more angle correction in the aortic data, which raises the possibility of overestimation of the angle-corrected aortic velocities.

TABLE 1
Serial velocity measurements (cm/sec) across atroioventricular valves in patients studied serially

<table>
<thead>
<tr>
<th>Weeks gestation</th>
<th>18–25</th>
<th>&gt;25–&lt;32</th>
<th>32-term</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>Max.</td>
<td>Mean</td>
<td>Max.</td>
<td>Mean</td>
</tr>
<tr>
<td>Tricuspid valve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. O.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.</td>
<td>59.3</td>
<td>12.3</td>
<td>46.6</td>
<td>8.3</td>
</tr>
<tr>
<td>Mean</td>
<td>55.0</td>
<td>15.9</td>
<td>44.0</td>
<td>12.5</td>
</tr>
<tr>
<td>S. P.</td>
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<tr>
<td>Max.</td>
<td>38.8</td>
<td>38.3</td>
<td>50.6</td>
<td>10.0</td>
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<tr>
<td>Mean</td>
<td>46.6</td>
<td>12.5</td>
<td>50.6</td>
<td>11.0</td>
</tr>
<tr>
<td>L. H.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.</td>
<td>43.7</td>
<td>57.7</td>
<td>70.0</td>
<td>50.1</td>
</tr>
<tr>
<td>Mean</td>
<td>44.0</td>
<td>13.5</td>
<td>13.9</td>
<td>44.6</td>
</tr>
<tr>
<td>W. W.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.</td>
<td>41.0</td>
<td>8.8</td>
<td>7.2</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>41.0</td>
<td>12.0</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>M. H.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max.</td>
<td>57.7</td>
<td>13.5</td>
<td>13.9</td>
<td>50.1</td>
</tr>
<tr>
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<td>14.5</td>
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<td>G. C.</td>
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<td></td>
</tr>
<tr>
<td>Max.</td>
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<td>13.9</td>
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<td></td>
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<tr>
<td>Mean</td>
<td>73.1</td>
<td>14.5</td>
<td></td>
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<tr>
<td>E. E.</td>
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<tr>
<td>Max.</td>
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<td>7.2</td>
<td></td>
<td></td>
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<tr>
<td>Mean</td>
<td>44.6</td>
<td>9.6</td>
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</tbody>
</table>

Doppler flow tracings in the atroioventricular valve inflow regions showed a dominant late diastolic component coincident with atrial systole. This may reflect the decreased diastolic compliance of the fetal heart14 and may explain the importance of atrial systole to normal cardiac function in the fetus. Both decreased compliance and right heart dominance might explain the development of right ventricular enlargement, ascites, and edema (hydrpos) in the fetus with a cardiac malfunction, since the right heart of the fetus handles the major portion of the volume load induced by severe anemia or abnormal cardiac rhythm.15

A substantial amount of error is potentially present in the method of calculation of volume flow. Even though annular diameters varied only about 1 mm, this could still represent a 20% error in diameter measurement in some of the smaller fetuses and might induce a
and may be helpful as an adjunct to the diagnosis of congenital heart disease.

This work provides a preliminary approach to defining normal velocities for application of Doppler techniques in the study of human fetal cardiac physiology.

References
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K L Reed, E J Meijboom, D J Sahn, S A Scagnelli, L M Valdes-Cruz and L Shenker

Circulation. 1986;73:41-46
doi: 10.1161/01.CIR.73.1.41

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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