Fetal Cardiac and Peripheral Arterial Flow Velocity Waveforms in Intrauterine Growth Retardation

Irene A.L. Groenenberg, MD, Jurij W. Wladimiroff, MD, PhD, and Wim C.J. Hop, MSc

Maximum flow velocity waveforms were studied at the cardiac level (ascending aorta, pulmonary artery, and ductus arteriosus) and at the peripheral level (fetal internal carotid artery, descending aorta, umbilical artery, and maternal uteroplacental artery) in 25 patients with intrauterine growth retardation and 25 normal control subjects matched for gestational age and maternal parity. Gestational age ranged from 27 to 35 weeks (median, 30 weeks). All flow velocity waveforms were obtained with a mechanical sector scanner combined with a pulsed and continuous Doppler system with a carrier frequency of 3.5 and 3.0 MHz. Normal pregnancy was characterized by low fetal and placental vascular resistances. The peak systolic velocity in the ascending aorta was significantly higher compared with the pulmonary artery. In patients with intrauterine growth retardation, reduced end-diastolic flow velocities were documented in fetal descending aorta, umbilical artery, and maternal uteroplacental artery, reflecting raised umbilical placental and uteroplacental vascular resistances. Raised end-diastolic flow velocities were observed at the cerebral level, reflecting reduced cerebral vascular resistance (“brain-sparing” effect). Reduced peak systolic flow velocities documented at the cardiac level may be secondary to reduced volume flow, increased valve or vessel size, or raised afterload. The noninvasive nature of this study did not allow differentiation between these variables. (Circulation 1989;80:1711–1717)

Previous work on fetal hemodynamic function has centered mainly on the lamb. Two-dimensional real-time and Doppler ultrasound makes possible noninvasive examination of the human fetal cardiovascular system. Doppler studies of the fetal umbilical and maternal uteroplacental artery have been reported to identify fetuses at risk for intrauterine growth retardation (IUGR) and poor fetal outcome.1–4 Reduced end-diastolic flow velocities in the fetal umbilical, aortic, and maternal uteroplacental arteries have been associated with increased peripheral vascular resistance, indicating impaired placental perfusion.2,5–7 However, reports on the effect of this increase in afterload on the fetal heart have been contradictory. Both increased right ventricular cardiac output8 and decreased9 combined ventricular cardiac output have been documented in the absence of end-diastolic flow in the umbilical artery.

The purpose of the present study was twofold: first, to document the changes in cardiac and peripheral arterial blood flow velocity waveforms in the growth-retarded fetus according to a matched controlled study design; second, to relate these flow velocity waveform changes to placental disease.

Methods

IUGR was diagnosed in 25 singleton pregnancies at 27–35 weeks of gestation (median, 30 weeks) when the fetal abdominal circumference was below the fifth percentile for gestational age.10 The preg-

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FIGURE 1. Top panel: Two-dimensional five-chamber view of the human fetal heart with Doppler flow velocity waveform tracings from the ascending aorta (see arrow) during normal pregnancy (a) and intrauterine growth retardation (IUGR) (b). Middle panel: Two-dimensional short-axis and pulmonary arterial view of the human fetal heart with Doppler flow velocity waveform tracings from the pulmonary artery (see arrow) during normal pregnancy (a) and IUGR (b). CR, cranial; CA, caudal. Bottom panel: Two-dimensional short-axis view of the human fetal heart parallel to the fetal spine with Doppler flow velocity waveform tracings from the ductus arteriosus (see arrow) during normal pregnancy (a) and IUGR (b).

a previously normotensive woman. In preeclampsia, pregnancy-induced hypertension is accompanied by proteinuria of 300 mg/l or more. In the remaining seven pregnant women, no cause for the IUGR could be established. Twenty-five normal singleton pregnancies with the fetal abdominal circumference between the fifth and 95th percentile for gestational age served as matched controls. Matching took place with respect to gestational age and maternal parity. Maternal age in the normal group varied between 19 and 39 years (median, 26 years). In the IUGR group, fetal birth weight was below the fifth percentile, and in the normal control group, fetal birth weight was between the 10th and 95th percentile according to Kloosterman’s Tables corrected for maternal parity and fetal sex. The study protocol was approved by the Hospital Ethics Committee. All pregnant women consented to participate in the study.

A combined mechanical sector and pulsed-continuous Doppler system (Diasonics CV 400, Diasonics Inc, Mulpikas, California) with a carrier frequency of 3.5 and 3.0 MHz was used. The sector scanner operates at power outputs of less than 100 mW/cm² spatial peak-temporal average in both imaging and Doppler modes by manufacturer’s specifications. Two-dimensional real-time imaging was needed to position the Doppler sample volume in the region of interest. Maximum flow velocity waveforms were recorded at both cardiac and peripheral levels. Each patient was included in the study only once. Doppler studies were performed by one examiner (I.A.L.G.). At cardiac level, Doppler recordings were produced from the fetal ascending aorta, pulmonary artery, and ductus arteriosus. Flow velocity waveforms from the fetal ascending aorta were obtained from the five-chamber view (Figure 1). Fetal pulmonary artery flow velocity waveforms were recorded from the conventional echocardiographic short-axis view (Figure 1). Doppler sample volumes were placed in the great vessels immediately distal to the semilunar valves. Flow velocity waveforms from the fetal ductus arteriosus were obtained from the short-axis view distal to the
pulmonary artery\(^\text{13}\) (continuous Doppler) (Figure 1). The angle between the Doppler cursor and the assumed direction of flow was always 5° or less. Sample volume length was between 0.1 and 0.3 cm. The correct position of the pulsed Doppler gate was ensured by two-dimensional ultrasound before and after each Doppler tracing was obtained. Peak systolic velocity (cm/sec) was determined in all three cardiac vessels studied.

Peripheral arterial Doppler studies were focused on the maternal uteroplacental artery, the lower thoracic part of the fetal descending aorta and fetal umbilical artery representing the uteroplacental and umbilical placental circulation, and the fetal internal carotid artery representing cerebral blood flow. In each instance, the procedure consisted of location of the vessel of interest followed by recording of the arterial flow velocity waveform. By placing the two-dimensional real-time transducer over the outer margin of the uterus nearest to the placenta, the maternal common iliac artery is visualized where it bifurcates into the external and internal iliac arteries. With the continuous wave Doppler transducer directed more medially, a uteroplacental artery in the lateral uterine wall may be identified.\(^1\) Doppler signals from this vessel are in the opposite direction to those from the iliac arteries\(^1\) and were always recorded on the placental side (Figure 2). The flow velocity waveform in the umbilical artery was obtained from a free-floating loop of the umbilical cord\(^\text{14}\) in both the presence of normal and reduced amounts of amniotic fluid (Figure 2). Flow velocity waveforms from the lower thoracic part of the fetal descending aorta were recorded from a sagittal cross section through the fetal trunk, displaying a major section of the fetal spine\(^\text{15}\) (Figure 3). Fetal internal carotid artery flow velocity waveforms were documented on a transverse cross section through the lower part of the fetal cerebrum showing a heart-shaped cross section of the brain stem with the anterior lobes representing the pedunculi cerebri.\(^\text{16}\) Anterior to this heart-shaped structure and, on either side of the midline, an oblique cross section of the internal carotid artery as it divides into its middle and anterior cerebral branches can be seen (Figure 3). The tortuous or curved course of the maternal uteroplacental, umbilical, and fetal internal carotid arteries did not allow positioning of the Doppler cursor parallel to the direction of blood flow, thus rendering impossible an accurate determination of the angle of incidence between flow and the Doppler beam and calculation of absolute velocities. Instead, angle-independent indexes expressing the pulsatility of the arterial flow velocity waveform were calculated. For the maternal uteroplacental artery, this was the end-diastolic to peak systolic flow velocity ratio (EDV/PSV ratio), and for the remaining peripheral vessels, this was the pulsatility index.\(^\text{17}\) The pulsatility index is derived by dividing the difference between peak systolic and end-diastolic velocity by the mean flow velocity over the entire cardiac cycle. Both EDV/PSV ratio and pulsatility index mainly reflect downstream impedance as has been shown in animal\(^\text{17,18}\) and human studies.\(^\text{6}\) In fetal lambs, embolization of the umbilical placental circulation has been performed to increase placental flow resistance and to observe the effect on the umbilical artery\(^\text{7}\) and fetal descend-
ing aorta flow velocity waveform.\textsuperscript{18} A reduction in end-diastolic flow velocity was established in both vessels together with a rise in calculated vascular resistance. In human pregnancy,\textsuperscript{6} reduced end-diastolic flow velocities in the umbilical artery were associated with a loss of small arteries in the tertiary villi of the placenta.

All Doppler studies at cardiac and peripheral levels were performed with the patient in the semi-recumbent position and during periods of fetal apnea because high-amplitude fetal breathing movements modulate blood flow velocity waveforms.\textsuperscript{19}

All flow velocity waveforms were recorded on hard copies. A microcomputer (Olivetti M24, Olivetti BV, Leiden, The Netherlands) linked to a graphics tablet was used for analysis of the Doppler recordings. An average of four consecutive flow velocity waveforms with the highest velocity and of similar appearance was used to establish each value.

Within the IUGR group, all Doppler flow velocity waveforms were recorded within 14 days of delivery (median, 4 days), thus allowing assessment of the relation between these flow velocity waveforms and the percentage of placental infarction. For this, the placentas were cut into slices of 0.5 cm each. The number and dimensions of the areas of infarction were defined through macroscopic examination, and the percentage of placental infarction was subsequently calculated.

Statistical analysis of the data consisted of the Wilcoxon matched-pairs signed-ranks test for comparing the Doppler data from the IUGR patients with data from the matched control subjects. Comparison of the Doppler data from the IUGR patients with the degree of placental infarction was performed by calculation of the correlation coefficient. Multiple regression was used to simultaneously investigate the relation of the various Doppler measurements with the percentage of placental infarction. Statistical significance was tested at the level of 0.05.

Results

Doppler Data From Patients With Intrauterine Growth Retardation Compared With Normal Control Subjects

Tables 1 and 2 present the peripheral and cardiac flow velocity waveform values in IUGR patients and normal control subjects. In normal pregnancy, high-forward velocity levels are maintained throughout end diastole in the maternal uteroplacental artery, umbilical artery, fetal descending aorta, and fetal internal carotid artery. In IUGR, a statistically significant reduction of peak systolic velocity in all three cardiac vessels as well as the pulsatility index from the fetal internal carotid artery and EDV/PSV ratio from the maternal uteroplacental artery was documented. A statistically significant rise was observed for the pulsatility index from the umbilical artery and fetal descending aorta. Six cases of IUGR ended in intrauterine death before 30 weeks of gestation. The flow velocity waveforms from these cases did not significantly differ from those of the surviving IUGR cases of similar gestational age.
Both during normal pregnancy and IUGR, the peak systolic velocity in the fetal ascending aorta was significantly higher than that in the pulmonary artery. There was no significant difference in mean fetal heart rate (beats/min) between normal pregnancies (median 141; range, 123–157) and cases of IUGR (median 145; range, 125–155).

**Doppler Data From Patients With Intrauterine Growth Retardation Relative to Degree of Placental Infarction**

The percentage of placental infarction ranged from 0% to 50% (median, 15%). A significantly positive correlation was established between the percentage of placenta infarction and pulsatility index from the fetal descending aorta ($r=+0.53$, $p=0.02$) and umbilical artery ($r=+0.69$, $p=0.001$). A significantly negative correlation was present between the percentage of placental infarction and the EDV/PSV ratio in the maternal uteroplacental artery ($r=-0.60$, $p=0.005$) as well as the peak systolic velocity ($r=-0.49$, $p=0.03$) in the fetal pulmonary artery.

Multiple regression analysis, also taking into account gestational age, revealed that the strongest correlation with the percentage of placental infarction was displayed by the pulsatility index from the umbilical artery and the EDV/PSV ratio from the maternal uteroplacental artery.

**Discussion**

Normal pregnancy is characterized by a low fetal and placental vascular resistance. In the presence of IUGR, there is an elevated pulsatility index in the fetal descending aorta and umbilical artery and a reduced EDV/PSV ratio in the maternal uteroplacental artery resulting from a reduction in end-diastolic flow velocities and reflecting increased umbilical placental and uteroplacental vascular resistance. These data can be viewed as an indication of impaired uteroplacental perfusion.2–5. The reduced pulsatility index values in the fetal internal carotid artery suggest reduced cerebral vascular resistance, that is a “brain-sparing” effect as a result of fetal circulatory centralization in the presence of IUGR.16,20

At the cardiac level, Doppler flow velocity waveforms have been previously recorded across the atrioventricular valves8,21–24 and in the outflow tract.9,23,24 In the present study, flow velocity waveforms were successfully recorded in the fetal ascending aorta and pulmonary artery in 100% and in the fetal ductus arteriosus in 92% of the IUGR patients.

In normal pregnancy, the mean peak systolic velocity in the ascending aorta and pulmonary artery was not essentially different from that reported by other investigators.13,21 Peak systolic velocities in ductus arteriosus depicted a wide scatter as has been established by other investigators13,22 the mean peak systolic velocity being nearly 100 cm/sec. In IUGR patients, peak systolic flow velocities were markedly reduced in all three cardiac vessels. For the ascending aorta and pulmonary artery, a similar reduction in peak systolic velocity was established.

Peak systolic flow velocity at cardiac valve level is a function of the flow through the valve and

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### Table 1. Peripheral Flow Velocity Waveform Values in Patients With Intrauterine Growth Retardation and Normal Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>Normal group (n=25)</th>
<th>IUGR group (n=25)</th>
<th>Significance of difference (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Range</td>
</tr>
<tr>
<td>EDV/PSV ratio maternal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uteroplacental artery</td>
<td>0.65</td>
<td>0.05</td>
<td>0.56–0.74</td>
</tr>
<tr>
<td>PI umbilical artery</td>
<td>1.05</td>
<td>0.16</td>
<td>0.74–1.49</td>
</tr>
<tr>
<td>PI fetal internal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carotid artery</td>
<td>1.66</td>
<td>0.25</td>
<td>1.14–2.43</td>
</tr>
<tr>
<td>PI fetal descending aorta</td>
<td>1.65</td>
<td>0.26</td>
<td>1.15–2.05</td>
</tr>
</tbody>
</table>

IUGR, intrauterine growth retardation; EDV/PSV, end-diastolic volume to peak systolic volume ratio; PI, pulsatility index.

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### Table 2. Cardiac Flow Velocity Waveform Values in Patients With Intrauterine Growth Retardation and Normal Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>Normal group (n=25)</th>
<th>IUGR group (n=25)</th>
<th>Significance of difference (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Range</td>
</tr>
<tr>
<td>Fetal ascending aorta</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak systolic velocity (cm/sec)</td>
<td>70.8</td>
<td>6.3</td>
<td>60.9–85.9</td>
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<tr>
<td>Fetal pulmonary artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak systolic velocity (cm/sec)</td>
<td>60.8</td>
<td>4.7</td>
<td>53.3–74.7</td>
</tr>
<tr>
<td>Fetal ductus arteriosus*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak systolic velocity (cm/sec)</td>
<td>97.4</td>
<td>11.0</td>
<td>76.7–119.0</td>
</tr>
</tbody>
</table>

* $n=23$. 
cross-sectional area of the valve. Peak systolic flow velocity is influenced by various factors such as preload, afterload (including arterial pressure and vascular resistance), heart rate, and the intrinsic contractile properties of the left and right ventricle. The human fetal model does not allow differentiation between all these factors. One may speculate that the higher peak systolic velocities in the ascending aorta compared with the pulmonary artery observed in normal pregnancy may be due to decreased fetal cerebral vascular resistance with subsequently lower left ventricular afterload. Based on time to peak velocity measurements in the ascending aorta and pulmonary artery, it has been suggested that in normal human fetuses between 16 and 30 weeks old, the mean pressure in the pulmonary artery is higher than that in the ascending aorta, which reflects a difference in resistance between the two circuits. Alternatively, the peak systolic velocity differences observed in our own study may well be determined by the difference in semilunar valve area between the two vessels.

Several explanations can be offered for the etiology of decreases in peak systolic flow velocity in the cardiac outflow tract in IUGR. Because volume flow is equal to mean velocity multiplied by area and because peak systolic velocity correlates to some extent with mean velocity, a decrease in peak systolic velocity could be secondary to a decrease in volume flow. Peak systolic velocity might also be lower if the valve of vessel through which blood is flowing increased in size, even if a volume flow were maintained or even increased. Changes in contractile function of the ventricle could also result in changes in peak systolic velocity, although tricuspid valve regurgitation was not observed in any of the IUGR patients. In addition, the afterload that is determined by blood pressure and resistance may play a role. Our Doppler studies at umbilical placental and uteroplacental level suggest an increase in resistance in these locations. However, both volume flow and pressure may change (in parallel or opposite directions) and result in alterations in the Doppler flow velocity waveform. Moreover, the waveform may not change with afterload if other factors change simultaneously. Again, differentiation between these explanations is not possible in the present model.

Within the IUGR group, umbilical artery pulsatility index was negatively related and maternal uteroplacental artery EDV/PSV ratio values were negatively related to the degree of placental infarction. This is in support of both fetal lamb data in which reduced end-diastolic flow velocities in the umbilical artery, resulting in raised pulsatility index values were documented after embolization of the umbilical placental circulation and human data in which similarly abnormal umbilical artery waveforms were associated with a loss of small arteries in the tertiary villi of the placenta. The degree of placental infarction exhibited a negative relation with peak systolic flow velocity in the pulmonary artery, whereas no such relation could be shown for the peak systolic flow velocity in the ascending aorta. One can only speculate on the etiology of these conditions. Extensive placental vascular infarction is associated with a significantly raised placental vascular resistance that may result in an increased afterload to both ventricles. The afterload to the left ventricle is not only determined by the vascular resistance at fetal trunk and placental level but also by cerebral vascular resistance, which appears to be reduced (brain-sparing) in IUGR. However, other variables influencing peak systolic velocity may also have played a role in this relation.

Our cardiac flow velocity data do not provide information on cardiac output and therefore do not allow comparison with other cardiac Doppler studies in which volume flow calculations at atrioventricular and outflow tract levels have been performed. Contradictory data have appeared on fetal cardiac output varying from increased right ventricular output to reduced combined output in the presence of abnormal umbilical artery waveform tracings. Some of this discrepancy may be due to the fact that Reed et al. corrected for fetal weight, whereas Al-Ghazali et al. did not. If fetuses are small for their gestational age, they might have decreased cardiac output for age at the same time that they have increased cardiac output for weight. Moreover, a substantial amount of error is potentially present in the method of calculation of fetal volume flow, particularly in smaller fetuses.

In conclusion, our results show that normal pregnancy is characterized by a low fetal and placental vascular resistance, whereas in IUGR there appears to be a raised resistance at umbilical placental and uteroplacental levels with reduced resistance at cerebral level (brain-sparing effect). The reduced peak systolic flow velocities at cardiac level in IUGR may be secondary to reduced volume flow, increased valve or vessel size or raised afterload. The noninvasive nature of the present model does not allow differentiation between these variables.

References


**KEY WORDS** • pulsatility index • peak systolic velocity • brain-sparing effect • placental vascular resistance
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