Editorial Comment

Doppler Ultrasound Studies of Human Fetal Blood Flow

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Previously, assessment of the health of the human fetus has been restricted to physical examination of the pregnant uterus within the maternal abdomen, auscultation of the fetal heart, and maternal perception of fetal movement. Interest in fetal health was limited not only by available technology but also by the relative inability to alter the natural history of an abnormal pregnancy or to support a preterm infant. With improved surgical, anesthetic, and neonatal support techniques came increased sophistication in methods of fetal examination. The practice of obstetrics was revolutionized by the ability to use ultrasound to detect congenital anomalies and growth abnormalities during prenatal life; intrapartum monitoring of the fetal heart rate and detection of patterns associated with hypoxia allowed early intervention in cases of fetal distress.

Techniques of fetal assessment continue to evolve, as demonstrated by the study in this issue of Circulation by Groenenberg and colleagues.\(^1\) By using two-dimensional ultrasound to measure fetal growth and Doppler ultrasound to measure velocities of blood in both the peripheral and the central circulation, the authors demonstrate how anatomic and physiologic information can be combined to provide a more complete picture of the cardiovascular derangements associated with the development of fetal intrauterine growth retardation.

The fetus is highly dependent on the supply of oxygen and nutrients from the placenta, and examination of the blood flow through the umbilical vessels was considered to have great potential for the assessment of fetal health. Most studies with Doppler in the umbilical vessels have examined arterial waveforms.\(^2,3\) The placenta is normally a low-resistance circulation; forward flow occurs in all phases of the cardiac cycle. As placental resistance increases, proportionately less flow occurs during diastole; thus, an index of placental function may be developed from the relative velocities of umbilical arterial blood flow during systole and diastole. Measurement of absolute blood velocity and volume flow from the fetus to the placenta requires knowledge of the angle between the Doppler beam and the direction of blood flow, along with measurements of the cross-sectional area of the umbilical artery. Both the angle and the vessel measurements are difficult to obtain with accuracy, and most investigators rely on indexes of umbilical artery blood flow that are angle independent. In normal fetuses as gestational age advances, the relative amount of blood flow during diastole increases relative to systolic flow, and index measurements of umbilical artery blood flow decrease.\(^2,3\) This decrease in the umbilical artery blood flow index suggests that placental resistance decreases with gestational age, a finding reported in studies in fetal lambs.\(^4\)

Doppler examinations have also been performed on the descending aorta\(^5,6\) and the intracerebral vessels in the fetus.\(^7-10\) Again, due to the problems of angle determination and cross-sectional vessel measurement, angle independent indexes derived from measurements are used for analysis.

The fetus with growth retardation is at increased risk for intrauterine or intrapartum death or for neonatal mortality or morbidity.\(^11\) Early identification of the fetus with abnormal growth allows increased surveillance and early delivery if distress is present. Some fetuses identified as small by ultrasound are relatively normal and benefit from maintenance in utero, allowing the lungs and other organ systems to mature. For other fetuses, the intrauterine environment is so marginally supportive that the risk of intrauterine death or irreversible damage outweighs the risk of prematurity. A test or group of tests, particularly of a noninvasive nature, that could distinguish the stable fetus from the fetus developing irreversible morbidity would be of great

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use in perinatal medicine. Complicating any study
of the fetus with growth retardation is the variety
of definitions of abnormal growth, ranging from weight
less than the 10th percentile for gestational age to
weight less than the fifth or third percentile to
abnormal ratios of weight to height; all measure-
ments normally vary in different populations and
geographical locations.11

In the study by Groenenberg et al,1 blood flow
velocity waveforms in the umbilical artery, internal
carotid artery, and descending aorta in normal
fetuses are compared with waveforms in fetuses
with intrauterine growth retardation. As this group
and others have previously shown, the fetus with
growth retardation has a higher umbilical artery
blood flow index (in this case, the pulsatility index),
a higher descending aorta blood flow index, and a
lower internal carotid artery blood flow index when
compared with normal.2,3,5–10 These findings are
compatible with an increase in placental and periph-
ereal resistance and a decrease in intracerebral resis-
tance in the fetus with growth retardation.

Index measurements in the maternal uteroplac-
cental circulation were also examined with Doppler
ultrasound by Groenenberg and colleagues.1 Maternal
diastolic flow was relatively decreased in the
group of fetuses with growth retardation. Results
from other studies have shown similar changes in maternal uteroplacental circulation,
although values from normal and abnormal pregnan-
cies overlap, possibly because blood flow occurs
in short vessels over a wide area that is difficult to
sample with consistency.2,3,12

In the fetal heart, both ventricles eject blood into
the systemic circulation simultaneously; blood flows
through the heart in parallel rather than in series as
is normal in extrauterine life. Doppler studies in the
human fetal heart have demonstrated that right
ventricular blood flow is usually about 30% greater
than left ventricular blood flow.13–17 Tricuspid valve
velocities and diameters are greater than mitral
valve velocities and valve diameters. Pulmonary
artery velocities are lower than aortic valve veloc-
ities; the higher right ventricular volume flow com-
pared with left ventricular volume flow is accounted
for by the fact that the pulmonary valve is propor-
tionately larger than the aortic valve. Errors may
occur in the measurement of velocity because it
requires knowledge about the angle of incidence
between the Doppler beam and the estimated direc-
tion of flow. Errors may also occur in calculation of
volume flow, a product of mean temporal velocity
and cross-sectional area through which blood is
flowing. Most fetal valves are between 2 and 10 mm
in diameter; area is calculated from a diameter near
the limits of ultrasound resolution that is then
halved and squared, and a large error range is
possible in the ultimate volume-flow calculation.

Hypoxia is considered an important cause of
intrauterine growth retardation.11 Studies of blood
flow in animal fetuses with acute hypoxia or with
growth retardation induced by chronic hypoxia have
shown that blood flow increases to the brain, heart,
and adrenal glands and decreases to the musculo-
skeletal system, kidneys, spleen, gut, and lungs.18–21
The decrease in blood flow to most of the fetal body
and increase in blood flow to the fetal head is
believed to account for the differential in growth
failure seen in clinical practice; fetal head growth is
usually maintained at relatively normal rates until
late in the process of growth retardation. This is
referred to as the "brain-sparing" effect of circu-
tory changes in fetal growth retardation. Alterations
in the central circulation, with a decrease in right
ventricular output compared with left ventricular
output, could account for some of the differences in
peripheral circulation in fetuses with growth retar-
dation. Alternatively, hypoxia may result in ductal
dilation and pulmonary hypertension; fetal right
ventricular output may increase compared with left.
Another possibility is that the fetus with growth
retardation may alter ductus venosus and right
atrial streaming of the most highly oxygenated
blood returning from the placenta into the left
atrium and ventricle22,23 without major shifts in
relative right and left ventricular outputs. It may
also be that in the face of higher resistance in the
placenta, blood flow follows the path of least resis-
tance into the fetal brain, again without shifts in
relative right and left ventricular outputs.

Groenenberg et al1 measured peak velocities
through the pulmonary artery, aorta, and ductus
arteriosus in normal and growth-retarded fetuses.
They obtained these velocities within 5° of the
direction of blood flow, a difficult task in the fetus
that often assumes intraterine positions subopti-
mal for Doppler examinations. They found that in
both groups of fetuses, peak velocity in the aorta
exceeded peak velocity in the pulmonary artery.
Systolic velocities in the pulmonary artery, ductus
arteriosus, and aorta in growth-retarded fetuses
were lower than normal velocities, the significance
of which is unclear.

The velocity and contour of blood flow in the
heart and great vessels is the result of multiple
factors, including heart rate, volume flow, chamber
and myocardial stiffness, ventricular relaxation
properties, and peripheral resistance. Velocities will
also vary with the cross-sectional area through
which blood is flowing. Although it is possible to
attribute a decrease in peak velocities through the
great vessels to an increase in resistance to flow, a
change in systolic velocity may result from a variety
of factors other than resistance.

Results from other studies of intracardiac Doppler
velocities in fetuses with growth retardation have
varied. Aortic peak and mean velocities were
reduced in fetuses with absent end-diastolic veloc-
ities in the umbilical artery, a condition highly
associated with growth retardation and fetal or
neonatal morbidity and mortality.24 Volume flow
through the right ventricle was increased relative to
the left ventricle.\textsuperscript{24} An increase in the right ventricular internal diameter was reported in fetuses with growth retardation, as was an increase in the size of the ductus arteriosus.\textsuperscript{25} Others have reported a disproportionate lowering of pulmonary artery velocities and volume flow in growth-retarded fetuses such that the proportion of combined ventricular outflow fell from 58\% in normal fetuses to 47\% in growth-retarded fetuses.\textsuperscript{26}

It is probably an oversimplification to assume that each fetus with growth retardation will have consistent changes in Doppler velocities; it is more likely that alterations in flow vary with the etiology and stage of growth failure. Intracardiac Doppler waveforms in patients with various types of cardiac diseases have shown disparate patterns as the condition evolves from one stage to another; at some points, the waveforms may even appear normal.\textsuperscript{27} Rapid changes can be seen with medical therapy or hemodynamic alterations such as volume status, illustrating the dynamic nature of flow velocity patterns. Investigations in fetal lambs have demonstrated nonlinear responses to hypoxia.\textsuperscript{28} Due to the complex nature of fetal physiology and growth, it is, therefore, likely that testing of multiple regions of flow will be of better diagnostic value than will a single measurement such as an index of umbilical blood flow\textsuperscript{29} or peak velocity in a valve.

Doppler ultrasound has been used in fetal peripheral vessels to identify normal and abnormal flow velocity waveforms and to select fetuses that might benefit from increased surveillance. Doppler ultrasound has also been used to study the cardiovascular circulation of the normal and growth-retarded fetus; however, the significance of the results obtained so far has not been established, in part, because intracardiac Doppler velocities are affected by many variables in the cardiovascular system. The significance of the changes in intracardiac velocity in growth retardation remains to be addressed with studies that allow simultaneous measurements of pressure, volume flow, and resistance.

Ideally, future investigations will identify which Doppler measurements of the peripheral and central circulation have diagnostic and prognostic value in the assessment of fetal well-being. Serial measurements may prove to be particularly useful in the assessment of fetal effects of interventions such as maternal bed rest, oxygen administration, or medications. An understanding of the complex and dynamic nature of both the intrauterine environment and blood flow velocity waveforms is necessary for the interpretation of the observations made with this new method of fetal assessment.

References

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