Doppler Echocardiographic Studies of Deteriorating Growth-Restricted Fetuses

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Intrauterine growth restriction (IUGR) is associated with significant perinatal mortality and morbidity [1, 2]. Adequate management of this condition requires early recognition of small-for-gestational-age (SGA) fetuses, a differential diagnosis of the factors that induce a delay in growth, monitoring the fetal condition, and determining the time of delivery.

The differential diagnosis between these etiologies is complex, but the introduction of noninvasive (i.e., high-resolution ultrasound imaging and Doppler ultrasonography) and invasive (i.e., cordocentesis) techniques allows a differential diagnosis in most of the cases [3]. Doppler ultrasonography, by providing a unique tool with which to examine fetal and maternal circulations noninvasively, has greatly enhanced our knowledge of the circulatory adaptive mechanisms that occur with various complications of pregnancy including IUGR [4, 5]. In particular, the study of fetal intracardiac hemodynamics has clarified the pathophysiologic steps in progressive fetal deterioration, allowing better definition of the severity of fetal compromise. Accurate assessment of the fetal condition may have favorable effects on perinatal mortality and morbidity, as fetuses can be delivered before irreversible damage occurs. In this chapter we outline the importance of Doppler echocardiography for antenatal monitoring of IUGR fetuses, with special emphasis on the hemodynamic changes at the level of the fetal heart in the presence of progressive deterioration.

Pathophysiology

Although the pathophysiology underlying uteroplacental insufficiency is poorly understood, it is assumed that various maternal, uterine, placental, and perhaps fetal abnormalities cause a reduction in the supply of nutrients provided to the fetus through the placenta [5–7]. This situation induces Doppler-detectable modifications in various vascular districts. These changes may include increased impedance to flow at the level of the uterine arteries (believed secondary to failure or impairment of trophoblast invasion), which results in poor uteroplacental blood perfusion [8, 9]. Similarly, impedance to flows is usually increased in the umbilical artery, which is considered an expression of high placental vascular resistance due to a reduction in the number of small muscular arteries in the tertiary stem villi or their obliteration [10–12]. Other explanations, such as increased fetal blood viscosity or reduced arterial blood pressure, have not been excluded [13, 14]. Irrespective of the underlying cause, the increased impedance in the uterine or umbilical arteries results in reduced delivery of oxygen and placental substrates to the fetus [5]. This condition causes differential changes of arterial vascular resistances in the fetal circulation with vasodilatation at the level of the brain and myocardium and constriction at the muscular and visceral level, resulting in the brain-sparing effect [15–17], a phenomenon long recognized in animal models [18]. Thus during the first stage of the disease, the supply of substrates and oxygen to vital organs is maintained at near-normal levels despite an absolute reduction of placental transfer.

The temporal sequence of Doppler-detectable modifications during a pregnancy with developing IUGR is still unknown. Sometimes abnormal uterine artery velocity waveforms are the first Doppler-detectable sign [19]. IUGR may occur even in the presence of normal uterine artery velocity waveforms, suggesting an etiology primarily related to abnormal placental function. Similarly, there is no evidence as to whether the abnormalities in the umbilical artery occur earlier, simultaneously, or later than those in fetal vessels [20]. As already stated, despite the common denominator of a reduced supply of nutrients, IUGR has multiple etiologies that may involve the uterine circulation, placenta, or fetal circulation.

Persistence of nutritional deprivation leads to progressive deterioration of the fetal condition with further hemodynamic changes mainly affecting cardiac function [21, 22] and causing abnormalities in the venous system [23]. Additional modifications include abnormalities in fetal motor behavior and heart rate patterns [6, 24]. Finally, if the fetus is not delivered in due course, fetal death ensues.
General Principles of Doppler Echocardiography for Functional Study of Fetal Cardiac Function

Fetal Circulation

Fetal cardiac hemodynamics differ from that seen postnatally. During fetal life blood is oxygenated in the placenta and returns to the fetal body via the umbilical vein. Studies on chronically instrumented fetal lambs have shown that under physiologic conditions about 55% of umbilical venous blood bypasses the hepatic circulation, entering the inferior vena cava (IVC) directly via the ductus venosus [5, 25]. From the IVC this highly oxygenated blood preferentially streams through the foramen ovale into the left atrium, left ventricle, and descending aorta. In contrast, poorly oxygenated blood from the hepatic and superior vena cava circulations enters the right atrium and is almost completely directed through the tricuspid valve in the right ventricle and pulmonary artery [5, 25]. Because fetal blood is not oxygenated by the lungs an additional shunt (i.e., the ductus arteriosus) operates to bypass the pulmonary circulation, preferentially directing the right ventricular output to the descending aorta. As a consequence, both ventricles eject into the systemic circulation in parallel. The output of the left ventricle is directed through the ascending aorta to upper body organs, making the most highly oxygenated blood available to the heart and brain. The right ventricle ejects through the patent ductus arteriosus and the descending aorta to the lower body and placenta.

Doppler Echocardiographic Technique

The parameters used to describe fetal cardiac velocity waveforms differ from those used for fetal peripheral vessels. In the latter situation indices such as the pulsatility index (PI), resistance index (RI), and systolic/diastolic (S/D) ratio are used. These indices are derived from relative ratios between the systolic, diastolic, and mean velocities and are therefore independent of the absolute velocity values and the angle of insonation between the Doppler beam and the direction of the blood flow [5, 26].

Unlike measurements at the cardiac level, other measurements yield absolute values. Measurements of absolute flow velocities require knowledge of the angle of insonation, which may be difficult to obtain with accuracy. Errors in the estimation of the absolute velocity resulting from the uncertainty of angle measurement are strongly dependent on the magnitude of the angle itself. For angles less than 20° the error is reduced to practical insignificance. For angles greater than 20° the cosine term in the Doppler equation changes the small uncertainty in the measurement of the angle into a large error in the velocity equations [5, 26]. As a consequence, recordings should be obtained with the Doppler beam as parallel as possible to the bloodstream. Moreover, all recordings with the estimated angle greater than 20° should be rejected.

Color Doppler sonography may solve many of these problems by showing in real time the flow direction, thereby allowing proper alignment of the Doppler beam with the direction of the blood flow. To record velocity waveforms, pulsed-wave Doppler sonography is generally preferred to the continuous-wave Doppler technique because of its range resolution. During recordings the sample volume is placed immediately distal to the location being investigated (e.g., distal to the aortic semilunar valves to record the left ventricular outflow).

Parameters Measured

The parameters most commonly used to describe the cardiac velocity waveforms are the following: peak velocity (PV), expressed as the maximum velocity at a given moment (e.g., systole, diastole) on the Doppler spectrum; time to peak velocity (TPV), or acceleration time, expressed by the time interval between the onset of the waveform and its peak; and the time velocity integral (TVI), calculated by planimetrizing the area underneath the Doppler spectrum.

It is possible also to calculate absolute cardiac flow from the atrioventricular and outflow tracts by multiplying the TVI × valve area × fetal heart rate (HR). These measurements are particularly prone to errors mainly because of inaccuracies in the valve area. The area is derived from the valve diameter, which is near the limits of ultrasound resolution; this figure is then halved and squared during the calculation, thereby amplifying any potential error. The measurements can be used properly in longitudinal studies for a short time interval during which the valve dimensions are assumed to remain constant. Furthermore, it is also possible to calculate accurately the relative ratio between the right and left cardiac outputs (RCO/LCO), thereby avoiding measurement of the cardiac valve: The relative dimensions of the aorta and pulmonary valves remain constant throughout the gestation in the absence of cardiac structural disease [27].

Recording Sites and Velocity Waveforms: Characteristics and Significance

In the human fetus blood flow velocity waveforms can be recorded at all cardiac levels, including venous return, foramen ovalis, atrioventricular valves, outflow tracts, and ductus arteriosus. Various factors af-