OBSTETRICS

Doppler ultrasonography in obstetrics: from the diagnosis of fetal anemia to the treatment of intrauterine growth-restricted fetuses

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After the adoption of the use of umbilical artery and middle cerebral artery peak systolic velocity in high-risk pregnancies and in pregnancies that are at risk of having an anemic fetus, the main focus of Doppler ultrasonography in obstetrics today is intrauterine growth-restricted fetuses. What is most needed at this time are (1) training of sonographers and sonologists on how to perform a Doppler study, (2) an international classification of intrauterine growth-restricted fetuses, and (3) a study of the natural history of intrauterine growth-restricted fetuses that might contribute to a better understanding of the intrauterine growth-restriction process and to standard treatment of intrauterine growth-restricted fetuses. Future investigations, which would include randomized studies, could be designed from the results of such studies.

Key words: Doppler assessment in obstetrics, ductus venosus, fetal anemia, IUGR, middle cerebral artery

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Doppler ultrasonography was introduced into obstetrics in 1977. In the first study of its kind, FitzGerald and Drumm[1] reported that umbilical artery (UA) waveforms are abnormal in fetuses with intrauterine growth-restriction (IUGR) and that reversed blood flow of the UA is associated with a poor prognosis. Their breakthrough concept of studying waveforms also resulted in several important clinical applications. For example, Doppler assessment of the UA has become standard for fetuses with IUGR; the Doppler assessment of the UA decreases perinatal mortality rates in high-risk pregnancies[2]; Doppler assessment has become part of the routine fetal echocardiography; and Doppler assessment of the middle cerebral artery (MCA) has become the standard of care for the diagnosis of fetal anemia, thus avoiding unnecessary invasive procedures.[3-6] Clearly, these are important achievements. But the question should be asked, "Is that all?" Is there a failing perhaps to recognize the real potential of Doppler assessment?

This clinical opinion article tries to answer these and other questions regarding controversial issues surrounding Doppler ultrasonography and addresses how Doppler studies and the analysis of the waveforms should be accomplished. It will also briefly discuss what has been learned from the diagnosis of fetal anemia with Doppler ultrasonography and review some of the new concepts regarding fetuses with IUGR that other investigators and my group have developed.

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Controversial issues

Doppler data that have been reported in the literature often seem to provide both technically and clinically contradictory results. For example, if the MCA pulsatility index (PI) is examined, we[7] and other investigators[8] have reported that the fetus loses the brain-sparing effect before death, but other investigators have not confirmed these results,[9] nor have they reported that this change can be very rapid and, therefore, not clinically useful.[10] Furthermore, some researchers have noted that the MCA PI has different patterns in fetuses with IUGR.[11] Based on these studies, it is presumably wise to conclude that fetuses with IUGR behave in different ways and that a single pattern cannot be generalized for the entire IUGR population. Although this would seem the logical conclusion, further experimental confirmation of this view is desirable.

Another example of uncertainty is represented by the maternal uterine arteries in the prediction of preeclampsia or IUGR.[12] A well-done review of the literature recently reported that abnormal uterine artery waveforms are a better predictor of preeclampsia than of IUGR, when performed after 16 weeks of gestation.[13] However, different indices best predicted preeclampsia or IUGR based on the a priori risk. Thus, an abnormal PI and uterine artery notching in the second trimester best predicted preeclampsia, whereas the best predictor of IUGR in high-risk patients was an increased resistance index. However, it still remains unclear (1) when the assessment of uterine arteries should be carried out (at 16, 20, or 24 weeks of gestation), and (2) whether assessment of the maternal uterine artery notch is useful, whether the PI or resistance index is the most useful parameter, or whether the addition of the PI or resistance index of both maternal uterine arteries is necessary.

A third example of uncertainty is represented by the UA reversed flow (RF). In this condition, > 70% of the placental arteries are obliterated[14]; therefore, many practitioners deliver a fetus with IUGR when there is UA-RF. However, there are no data that show UA-RF to be an indicator for delivery. Twenty years ago, I thought that UA-RF was an indication for delivery, but a case in 1991 gave me pause. A patient with dichorionic twins (1 twin had IUGR and UA-RF) declined intervention at 28 weeks of gestation but remained on bed rest in the hospital and 5 weeks later delivered healthy twins. This case suggested that, in fetuses with IUGR with UA-RF the pregnancy may continue for several weeks. Since that time, we have confirmed these results in singleton pregnancies and today believe that UA-RF is not an indication for delivery, especially at gestational ages of < 32 weeks. Figure 1, A, shows a case of UA-RF that was present 23 days before fetal death, which occurred at 26 weeks of gestation. The umbilical cord was sampled in a free-floating segment. Figure 1, B, shows the same fetus at the same exam, with the UA sampled at the placental insertion. Figure 1, C, shows normal UA waveforms at the same gestational age. Figure 1, D, shows the UA waveforms 24 hours before delivery. At this time, there was nonreassuring fetal testing; the patient was given the option of delivery, and she declined it. This fetus was acidemic at birth. We have also learned that the interval between the appearance of UA-RF and IUFD is longer in twins, compared with singleton fetuses (unpublished data).

A final example of uncertainty is represented by information that was obtained through the ductus venosus (DV) waveforms. The DV originates from the umbilical vein and bypasses the liver (Figure 2, A). DV waveforms were first described by Kiserud et al[15] and are characterized by 2 peaks (Figure 2, B). The first peak is called *peak systolic velocity* (PSV) and corresponds to the highest velocity of the blood in systole; it is followed by a period of decreased velocity called *isovolumetric relaxation*. The second peak corresponds to the rapid filling of the ventricles. The nadir is called "a-wave" and corresponds to atrial contraction, but DV "a-wave" RF (Figure 2, C) is an abnormal finding. This parameter has gained so much popularity that, even without appropriate scientific evidence, investigators and practitioners started using DV-RF as an indicator for delivery.[16] More recently, a registry reported interesting data regarding fetuses with IUGR with a suggestion that the DV a-wave is a primary fetal cardiovascular parameter that affects neonatal outcome and, therefore, should require evaluation in a randomized management trial. However, a key question regarding this study was asked by Ghidini,[17] "How good is a test that becomes a predictor of outcome only within 24 hours of fetal compromise and only in a minority of cases?"

Years ago, it was my belief that the fetus should be delivered in the presence of DV-RF (a-wave RF). However, my ideas on this subject changed when I began at Wayne State University in Detroit and had patients with severe early IUGR who declined any interventions, but who consented to be followed with Doppler ultrasonography. Among these patients, it was surprising to find several fetuses with severe IUGR and DV-RF who delivered 3-4 weeks after the appearance of DV-RF and did well. Using this new information, I changed my approach and today do not necessarily deliver based on DV-RF; instead, before 32 weeks of gestation, I look at other changes that are occurring in the fetus.

The presence of DV-RF can be explained in light of the transitional phase recently described by Picconi et al.[18] Based on this study, when the DV is assessed longitudinally in fetuses with IUGR, the progression follows 3 steps: the first step is characterized by normal waveforms; the second step is characterized by a period in which there are normal and abnormal waveforms (Figure 2, C-D, were obtained in the same fetus at the same examination); the last step is characterized by persistent abnormal waveforms. The same author has also recently developed a new index for the analysis of the DV waveforms. This index is called the *SIA index* (S-wave/isovolumetric relaxation + a-wave) and allows a much more accurate prediction of fetal outcome, compared with a-wave RF alone.[19] Figure 2, E, shows a set of abnormal DV waveforms; in this case, the SIA index was 4.02. Based on the study by Picconi et al,[19] this SIA value is associated with an almost certain perinatal death because the IUGR process is too severe and the fetus should have been delivered earlier. Figure 2, F, shows blood flow velocity waveforms of the umbilical vein that were obtained soon after its entrance into the abdomen. Note that the DV has a blue color, which indicates the presence of RF at the DV. In the presence of DV-RF, the umbilical vein becomes similar to the waveform of a normal DV (Figure 2, F). The velocity, however, is much lower at the umbilical vein.

What are the vessels that sonographers and sonologists should be trained to examine?

By reviewing the fetal Doppler literature, most investigators would agree that these vessels are the UA, the fetal MCA, and maternal uterine arteries.

Where to sample the UA?

In the literature, different ways have been reported regarding how to sample the UA. Our group samples the UA in a free-floating umbilical cord segment; if there is RF, the UA is assessed (when it is possible) close to the placental insertion. The reason is that this segment of the UA is the last part of the UA that experiences RF. Therefore, UA-RF at the placental insertion is more severe than UA-RF that is present only at the fetal abdominal insertion. Although no other study has examined this point, this assertion comes from our experience in a longitudinal study that was performed on the sequential cardiovascular changes in fetuses with severe IUGR.[20] The most used index to quantify these waveforms is the PI, which is plotted on our reference range. An example of different UA waveforms that were obtained at different levels is reported in Figure 1, A and B.

Where to sample the MCA?

The MCA should be sampled soon after its origin from the internal carotid ar-