Editorial

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Ultrasound Doppler waveform assessment: the story continues

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Ultrasound Doppler waveform assessment of the fetal and placental circulatory systems have been studied extensively and successfully applied in clinical practice. These waveforms provide information on the presence and direction of flow, velocity profile, volume of flow and impedance to flow. As such, studies of these waves facilitate monitoring the fetal hemodynamic state as well as identifying circulatory responses to physiologic and pathologic maternal and fetal conditions in a non-invasive way. With the advancements in Doppler utilization in fetal medicine and the extensive research in the field in the past two decades, this technology has proven an invaluable tool of fetal surveillance. Indeed, it has gained wide acceptance and revolutionized the management and antenatal surveillance of several fetal conditions.

For example, the ability to screen fetuses at risk of developing fetal anemia from any etiology is currently based on Doppler measurement of the peak systolic velocity in the middle cerebral artery (MCA) [1, 2]. This screening technique has proved to be an excellent tool that accurately estimates the likelihood of moderate to severe fetal anemia [2, 3]. Furthermore, it was shown to be superior to the previously acceptable invasive methodology of assessing fetal anemia by measuring the amniotic fluid bilirubin levels (delta OD450) [4, 5]. Consequently, delta OD450 is rarely used in current practice and is actually no longer readily available in most laboratories. Indeed, MCA Doppler evaluation emerged as an elegant "game changing", user-friendly non-invasive technology which replaced the need for repeated invasive tests and thus had an enormous impact on the well-being of thousands of fetuses.

Likewise, Doppler evaluation has greatly improved the ability to diagnose surveille and manage clinical scenarios in fetuses with suspected growth restriction. The most utilized Doppler application is that of the umbilical artery which reflects the placental resistance (impedance) to flow throughout the fetal cardiac cycle. Normal diastolic flow in the umbilical artery is commonly used as a reassuring finding suggesting low risk for perinatal morbidity or mortality, thus, allowing for expectant management and delay of delivery to achieve fetal maturity [6]. On the other hand, placental insufficiency may lead to increase umbilical artery Doppler indices due to decreased end-diastolic blood flow suggesting increased risk to the fetus. Furthermore, poor placental function in severe cases may present with findings of absent or reversed end diastolic flow Doppler signal conferring a particularly high risk for adverse perinatal outcome and mortality [7–13]. In fact, Doppler evaluation of the umbilical artery in cases of fetal growth restriction (FGR) is the most well-studied form of fetal monitoring. Multiple randomized clinical trials, meta-analyses of these trials and a Cochrane review have persistently indicated that screening of at-risk fetuses using the umbilical artery Doppler resulted in improved outcomes with a significant reduction in perinatal mortality [14]. Subsequently, Doppler-related research has expanded to focus on detecting fetal hemodynamic adaptation mechanisms through evaluation of multiple vessels such as the MCA, cerbro-placental ratio (CPR), umbilical vein, aortic isthmus (AOI) and ductus venosus. These investigations provide several insights on the fetal hemodynamic adaptation and circulatory compensation to chronic hypoxia and nutrition deprivation state [15–22]. Such detailed assessment of the fetal hemodynamic adaptation status improves our ability to individualize and fine tune the surveillance frequency and management decisions in FGR [23].

In this issue, two original studies explore the potential use of Doppler ultrasound in specific scenarios in fetal medicine [24, 25]. Although these studies differ greatly in their technique, the vessel that they examine, the clinical application and results, they do share the desire to further improve the utilization of Doppler assessment in a meaningful way that hopefully improves fetal outcome.

The first study by Villalalin et al. was designed to investigate whether reverse flow in the AOI in late onset FGR (diagnosed after 32 weeks of gestation) is associated with adverse perinatal outcomes [24]. The physiological rationale is that blood flow in the AOI is affected by both the cerebral and the systemic resistances which it supplies. It is known that with progression of early onset FGR the increased placental resistance combined with decreased cerebral resistance (secondary to the "brain sparing" effect) results in alteration in the AOI flow that may become reversed from its normal antegrade direction.

Indeed, reversed AOI flow is thought to represent circulatory redistribution reflecting fetal hemodynamic decompensation [26, 27].

In this issue, Villalalin et al. compared pregnancy and perinatal outcomes such as the mode of delivery, indications for cesarean section, Apgar score at 5 min, umbilical artery pH, neonatal intensive care unit (NICU) admission, and composite neonatal morbidity, between late onset FGR (diagnosed after 32 weeks of gestation) with antegrade and those with reversed AOI flow. They performed Doppler surveillance of the AOI in 148 singleton FGR cases with mild Doppler abnormalities defined as umbilical artery pulsatility index (PI) >95th centile, MCA PI <5th centile or CPR < 5th centile. The authors did not find significant difference in any of these variables between the groups. Based on the negative results they concluded that Doppler evaluation of the AOI does not provide any clinically useful information for predicting the perinatal outcome or the tolerance to labor in late onset FGR with mild Doppler alterations [24]. Despite these negative findings this study is important as it points to the potential different pathophysiology or hemodynamic adaptation in late vs. early-onset FGR. It is already known that the common umbilical artery alterations seen in early-onset FGR may not present in late-onset FGR [28]. Indeed, evaluation of the MCA and CPR appears to be superior to umbilical artery Doppler in the subgroup of late-onset FGR. This study suggests that there are multiple factors affecting the flow in the AOI apart from brain sparing affect. More significantly, unlike prior data suggesting increased risk for cesarean delivery and poor neurodevelopmental status in early-onset FGR with reversed AOI flow, the current study provides clinical support that the direction of flow in the AOI may not provide reliable prognostic information in late-onset FGR [29, 30].

The second study in this issue sets the ground for potential new use of Doppler wave form technology which is the assessment of the fetal main pulmonary artery pressure (FMPAP) [25]. Sosa-Olavarria et al. evaluated the use of a previously reported Doppler technique used in adults to estimate the FMPAP and correlated it with gestational age. They utilized the formula by Dabestani et al. in 337 healthy fetuses with normal growth between 13 and 38 weeks of gestation by measuring the time interval from the onset of the systolic flow to the peak systolic velocity through the pulmonary valve, i.e.: acceleration time [31]. The authors found that the acceleration time was increased and FMPAP decreased with advanced gestational age. These findings are not surprising given that the fetal pulmonary vasculature has low impedance at term in preparation for postnatal life. A similar technique has been suggested for predicting fetal lung maturity [32]. In addition, it is consistent with previous data that evaluated the pulmonary artery pressure in the post-natal period by using a different Doppler based technique [33–36].

If this technique proves to be a reliable mode of assessment of the FMPAP, it may be used to identify potential abnormalities in the pulmonary artery pressure. Such evaluation has the potential to have clinical utility in screening pregnancies that may be at risk for developing neonatal pulmonary hypertension due to a variety of causes. As such, its role in predicting pulmonary hypertension in cases of fetal arrhythmias, suspected meconium stained amniotic fluid, structural malformations such as congenital diaphragmatic hernia, expected prematurity, exposure to medication which have been associated with pulmonary hypertension and more could be assessed.

Further research in the field may assist in fine tuning the use of Doppler assessment in different clinical scenarios. Both negative and positive studies will shape the future of this technique and better determine the clinical utility to assess the fetal and maternal circulatory systems and improve neonatal outcome.

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