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Commentary

Reflections illuminate antenatal detection of placental pathology

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Most human pregnancies have a relatively uneventful progression to birth, but a proportion are accompanied by vascular pathologies affecting either the maternal or fetal sides of the placenta, now respectively categorized as maternal vascular malperfusion (MVM) [1] and fetal vascular malperfusion (FVM) [2]. These pathologies may compromise fetal well-being and predispose to complications that include fetal growth restriction, stillbirth, perinatal stroke and postnatal cerebral palsy. Current antenatal detection of placental pathology with routine ultrasound screening is only moderately successful for MVM, and difficult to attain for FVM. Through a newly-developed analytic technique which quantifies the degree of wave reflection within arteries of the umbilical cord using Doppler velocity waveforms obtained during antenatal ultrasound screening, Cahill et al.[3] provide a potential means for not only improving antenatal detection of MVM, but also permitting antenatal recognition of FVM.

Routine non-invasive ultrasound screening is an important element in the antenatal detection of placental pathology. This screening includes evaluation of placental morphology and the features of both maternal (uterine artery) and fetal (umbilical artery) blood velocity waveforms acquired with the Doppler technique, with quantitation of the pulsatility of these vessels via a 'pulsatility index'. Although the umbilical artery pulsatility index may be increased in the presence of placental pathology, antenatal prediction of MVM in patients using routine ultrasound screening is only moderately successful, even when combined with a clinical risk score and maternal serum biomarkers [4]. Cahill et al. [3] have therefore sought to bolster diagnostic capability in this area via a more detailed analysis of the umbilical artery blood velocity waveform in patients classified as having MVM or FVM following examination of the placenta after birth.

The approach utilized by Cahill et al. [3] is grounded in well-established physiological principles [5]. Thus, contraction of the heart generates flow (and pressure) waves which travel down the arterial tree. During their propagation, these 'forward' waves are partially reflected back towards the heart wherever they encounter 'impedance mismatching', which may occur at branch points or other transitions in arterial size or stiffness. These reflected 'backward' waves then merge with forward waves to either augment or suppress flow, depending on the nature of the impedance mismatch, and thereby change the morphology of the overall blood velocity waveform. Using techniques analogous to those applied in electrical transmission line analysis, the measured 'net flow' waveform can be mathematically decomposed into its forward and backward wave components, with the degree of wave reflection quantifiable via a "reflection coefficient", calculated as the ratio of the magnitudes of backward and forward waves. An increasing body of evidence suggests that the reflection coefficient represents a measure of arterial health, with an elevated reflection coefficient being an independent predictor of both adverse cardiovascular events and mortality in adult population studies [6,7].

The conventional ultrasound approach for obtaining a non-invasive reflection coefficient in the arterial circulation of children and adults requires near-simultaneous measurement of a Doppler blood velocity waveform and a blood pressure waveform (or a surrogate such as the arterial diameter waveform) at a single site, followed by deconvolution of these waveforms into forward and backward components using established wave separation techniques [5]. However, for the less-accessible fetal circulation, Cahill et al. [3] employed a recently-developed approach which uses just the blood velocity waveform, but from two spatially separated measurement sites. In essence, this approach utilizes the change in morphology of measured Doppler blood velocity waveforms between the fetal and placental ends of the umbilical arteries (typically a distance of ~50 cm in humans) to derive the forward and backward wave components consistent with the observed change in morphology, thus permitting calculation of an umbilical arterial reflection coefficient [8].

Several findings in the study of Cahill et al. [3] are noteworthy. First, the average umbilical artery reflection coefficient of the MVM and FVM groups was higher than in control patients, with the increased reflection coefficient in MVM presumably secondary to the fetal consequences of vascular pathology affecting the maternal side of the placenta. However, while both the umbilical and uterine artery pulsatility index were elevated in the MVM group, neither was increased in the FVM group. Therefore, combining routine ultrasonography with assessment of the umbilical artery reflection coefficient may facilitate attaining the elusive goal of diagnosing FVM

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antenatally. Furthermore, the prediction of MVM or FVM with the umbilical artery reflection coefficient alone, although moderate (area under the curve or AUC = 0.78), was similar to the prediction of MVM previously reported with routine ultrasound screening combined with a clinical risk score and maternal serum biomarkers (AUC = 0.77) [4]. A pressing need of future, and hopefully larger, cohort studies is thus determination of the extent to which addition of the umbilical artery reflection coefficient to the mix can improve antenatal prediction of MVM beyond that currently provided by the clinical risk score, maternal serum biomarkers and routine ultrasonography.

Cahill et al. [3] are to be complimented for bringing the technique of arterial wave separation analysis, which has largely been a research tool to date, into the realm of antenatal clinical diagnosis. The potential benefits of this analysis for enhancing clinical outcomes in at-risk pregnancies will undoubtedly provide considerable impetus for larger population studies in this area.

Declaration of Competing Interest

The authors declare no conflicts of interest.

Authors' contribution

J. Smolich drafted the manuscript. J. Smolich and J. Mynard edited, reviewed it and approved final submission of the manuscript.

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