

## Is uterine artery Doppler velocimetry effective for prediction of pre-eclampsia and intrauterine growth restriction?

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Accurate prediction of high-risk pregnancies, such as pre-eclampsia and intrauterine growth restriction (IUGR), is crucial to allow judicious allocation of resources for monitoring and preventive treatment to improve maternal and perinatal outcomes. Pre-eclampsia and IUGR are characterized by abnormal placenta formation,<sup>1</sup> which results in inadequate uteroplacental blood flow. This has led to the idea of using Doppler ultrasonography to assess the velocity of uterine artery blood flow as part of routine ultrasound screening.<sup>2</sup>

During pregnancy, the uterine artery Doppler flow velocity waveform typically demonstrates a low pulsatility with a high end-diastolic pattern. This is due to trophoblastic invasion of the radial artery in the early placentation period, leading to a dramatic fall in vascular resistance. In normal pregnancies, the systolic/diastolic (S/D) value of uterine artery velocimetry is consistently  $2.0 \pm 0.4$  from 22 weeks gestation and beyond. However, in pre-eclampsia or IUGR, which is associated with incomplete invasion of trophoblasts, vascular impedance increases, thereby resulting in abnormal elevation of S/D.<sup>3-6</sup> Thus, when a pregnancy is associated with a S/D value of  $>2.6$ , the incidence of adverse fetal outcomes significantly increases when compared with that of normal S/D values.<sup>7</sup>

The presence of an early-diastolic notch in the uterine artery velocimetry waveform is another abnormal finding suggesting high impedance vascular flow. An early-diastolic notch is normally seen up to 24-26 weeks of gestation, then disappears. Our study showed that the prevalence of an early-diastolic notch beyond 28 weeks of gestation was approximately 3% and that the presence of an early-diastolic notch was highly associated with adverse pregnancy outcomes, such as cesarean section for fetal distress, IUGR, neonatal

intensive care unit admission, and poor perinatal outcomes. Furthermore, when the notch was categorized according to its depth using the notch index (NI=minimal velocity in early diastolic notch/maximal velocity in diastole), pregnancy outcome was significantly worse in the group with a deeper notch. Thus, it is not the presence of an end-diastolic notch *per se*, but its depth is clinically important in predicting adverse pregnancy outcomes.<sup>8</sup>

According to our study, the risks for adverse perinatal outcomes were increased when the uterine artery Doppler velocimetry was abnormal in the intermediate risk groups, such as those groups with borderline oligohydramnios (AFI 5-8) and those with an estimated fetal weight in the 10-25<sup>th</sup> percentiles. Abnormal uterine artery Doppler velocimetry, in addition, was useful for predicting IUGR and pre-eclampsia as well.<sup>9</sup>

In several studies, however, the positive predictive value of uterine artery Doppler velocimetry for predicting adverse pregnancy outcomes has been reported to be relatively low. The meta-analysis of Cnossen et al.<sup>10</sup> showed that although a pulsatility index, alone or combined with notching, is the most predictive Doppler index, most Doppler indices had poor predictive characteristics.

Thus, the addition of other clinical or biochemical parameters to uterine artery Doppler velocimetry increases the relatively low predictive value of uterine artery Doppler velocimetry alone. Nicolaides et al.<sup>11</sup> reported that maternal demographic characteristics, uterine artery Doppler velocimetry, and maternal mean arterial pressure provided a significant independent contribution in the prediction of pre-eclampsia, gestational hypertension, and small for gestational age. Thus, the combination of the above three factors is an effective screening tool for the prediction of pre-eclampsia. Furthermore,

the diagnostic performance of uterine artery Doppler velocimetry for predicting IUGR can be improved significantly when the degree of maternal weight gain until the mid-second trimester was simultaneously taken into account.<sup>12</sup> In addition, elevated levels of  $\alpha$ -fetoprotein,  $\beta$ - human chorionic gonadotropin, CRP, and cystatin C are reported to be useful in the identification of patients at risk for hypertensive disorders of pregnancy. Recently, several other predictive biochemical markers, including placental growth factor, soluble fms-like tyrosine kinase-1 (sFlt-1), plasma protein 13, and pregnancy associated plasma protein-A (PAPP-A), have been evaluated, but none of the markers are currently in routine clinical use since these markers also have limitations in predicting high risk pregnancies.

Although studies investigating the predictive accuracy of uterine artery Doppler indices for high-risk pregnancy have revealed considerably varied results, uterine artery Doppler ultrasonography has been shown to be a useful test in predicting high risk pregnancies secondary to uteroplacental insufficiency. Moreover, Doppler assessment is non-invasive and could be fairly easily performed at the time of a detailed anomaly scan. However, it is still questionable whether uterine artery Doppler ultrasonography should be used as a predictive test. Thus, in order to improve the predictive accuracy of uterine artery Doppler velocimetry, integrating other parameters of placental function or endothelial activation with uterine artery Doppler velocimetry can be considered.

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