OBSTETRICS

Assessment of uterine artery and aortic isthmus Doppler recordings as predictors of necrotizing enterocolitis

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OBJECTIVE: The purpose of this study was to evaluate whether changes of uterine arteries and aortic isthmus Doppler blood flow recordings could enhance the prediction of necrotizing enterocolitis.

STUDY DESIGN: Doppler characteristics of the uterine artery, umbilical and middle cerebral arteries, ductus venosus, and aortic isthmus were reviewed in 123 growth-restricted fetuses who were then divided into 2 groups: with and without necrotizing enterocolitis.

RESULTS: Twelve of 123 newborn infants (9%) expressed necrotizing enterocolitis. This group showed significant association between necrotizing enterocolitis and bilateral notching on the uterine artery (83.3% vs 29.7%; $P < .001$), uterine artery mean resistance index (83.3% vs 36.9%; $P < .002$), aortic isthmus diastolic blood flow velocity integrals (Z score: −7.32 vs −3.99; $P = .028$), and absent or negative "a" wave on the ductus venosus (17% vs 1.8%; $P = .021$). With the use of logistic regression, uterine bilateral notching could predict necrotizing enterocolitis with a sensitivity of 83.3% and a specificity of 70.3%.

CONCLUSION: More than any other variable, uterine bilateral notching should be recognized as a strong risk factor for necrotizing enterocolitis.

Key words: aortic isthmus, Doppler assessment, intrauterine growth restriction, necrotizing enterocolitis, uterine artery

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Necrotizing enterocolitis (NEC) affects up to 10% of children with placental circulatory insufficiency and intrauterine growth restriction (IUGR). It creates a mortality rate as high as 10%.[1,2] Identification of reliable prenatal predictors of NEC would allow the development of preventive measures that specifically would target neonates who are at risk and reduce morbidity and mortality rates that are related to this complication. Because of fetal hypoxemia, fetuses with IUGR show middle cerebral artery (MCA) vasodilation that is associated with peripheral vasoconstriction that also involves the mesenteric arteries.[3,4] Despite these hemodynamic disturbances, none of the usual arterial or venous Doppler variables could predict NEC clearly when logistic regression analysis was applied, and birthweight remains the predominant risk factor.[5,6] To our knowledge, 2 other vascular sites, namely the fetal aortic isthmus and the maternal uterine arteries, have not yet been investigated in this context with the same approach.

Because of the parallel disposition of the fetal ventricles, blood flow through the aortic isthmus reflects the balance between the resistances of the supra- and infradiaphragmatic circulations.[7] Patterns of aortic isthmic blood flow are now considered to be strong indicators of fetal hemodynamic status and have been related to perinatal outcome in IUGR.[8,9] In this condition, the increase in placental resistance causes a fall in umbilical blood flow and secondary hypoxemia that are responsible for cerebral vasodilatation. These hemodynamic changes, classically described as the brain-sparing effect, result in a decrease in the antegrade isthmic blood flow[8,10,11] and, for the most severe cases, in a retrograde blood flow that leads to ventricular dysfunction.[12] Mesenteric hypoxic vasoconstriction, which is another major element of this blood redistribution process,[3] should further increase the infradiaphragmatic vascular resistance and contribute even more to the decrease in antegrade isthmic blood flow.

In addition to the placenta, uterine perfusion is another determinant element of the maternofetal exchange. Isolated impairment of the normal fall of uterine vascular resistances that has been observed during gestation can lead to IUGR and chronic fetal hypoxemia that is associated with cerebral vasodilation and mesenteric vasoconstriction.[13]

The objective of this study was to evaluate whether Doppler assessment of uterine arteries (UtAs) and aortic isthmus blood flow could enhance prediction of NEC in a population of fetuses with IUGR and to assess whether low birthweight alone re-

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TABLE 1
Categoric Doppler characteristics of subjects with (group 1) and without (group 2) necrotizing enterocolitis

Variable	n (%)	χ^2	*P* value
Bilateral protodiastolic notch on uterine artery Doppler assessment			
Group 1	10 (83.3)	13.685	.001
Group 2	33 (29.7)		
Uterine artery resistance index >95th percentile			
Group 1	10 (83.3)	9.605	.002
Group 2	41 (36.9)		
Ductus venosus minimal diastolic blood flow (absent-retrograde)			
Group 1	2 (16.7)	9.605	.002
Group 2	4 (3.6)		
Aortic isthmus: absent or retrograde diastolic blood flow			
Group 1	8 (66.7)	1.884	.170
Group 2	49 (45.8)		

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mains a risk factor in absence of abnormal maternofetal exchanges.

Materials and Methods

Inclusion criteria

All fetuses that were referred to our unit for growth restriction (weight <10th percentile for age)[14,15] from January 2003 to September 2008 were eligible for the study. Pregnancies were dated by ultrasound examination from 16-18 weeks of gestation. After birth, the population was divided into 2 groups depending on whether NEC developed. The diagnosis of NEC was based on clinical (abdominal distension, bile aspirate, vomiting, or hematochezia) or radiologic (signs of perforation) manifestations. Pre- and postnatal data were compared between the 2 groups.

Exclusion criteria

Exclusion criteria included delivery outside our center, birthweight >10th percentile for gestational age, chromosomal abnormality, cardiac or extra cardiac malformations, fetal Doppler images that were recorded >1 week before birth.

Prenatal data

Echocardiographic examinations were performed with a Sequoia machine (Acuson, Mountain View, CA) with either a 5 or a 6 C2 MHz transabdominal transducer and were recorded on video tapes. Doppler recordings in UtA, umbilical artery, MCA, ductus venosus, and aortic isthmus are part of our routine investigation of fetuses with growth restriction. The last Doppler study was reviewed retrospectively by 2 independent observers (M-J.R., C.H.) who were unaware of the postnatal outcome; the outcome was used for analysis. The mean resistance index of the UtA was calculated with the average of the resistance indices of 3 consecutive waveforms on both arteries.[16] The presence of a bilateral notch was also reported for each UtA. The pulsatility index of umbilical artery was calculated at the fetal abdominal chord insertion and was considered abnormal when it was >95th percentile.[17] The aspect of umbilical artery diastolic blood flow was classified as normal, decreased, absent, or retrograde. The aortic isthmus blood flow had been recorded according to previous description; diastolic blood flow was classified as antegrade, absent, or retrograde.[18] Isthmic systolic and diastolic time velocity integrals (TVI) were obtained on 3 consecutive beats with an ultrasound angulation of <30 degrees. The isthmic blood flow index was then calculated with the following equation: isthmic blood flow index = (systolic TVI + diastolic TVI)/systolic TVI.[19] For the ductus venosus, we traced the time-averaged maximum velocities of 3 consecutive complexes and reported the minimal velocity during atrial contraction (A wave) and the pulsatility index. The blood flow in the ductus venosus during atrial contraction (A wave) was classified as antegrade, absent, or retrograde.

Postnatal data

The postnatal data charts of the children and mothers were reviewed. For the latter, we looked for the presence of maternal high blood pressure and/or preeclampsia. *Pregnancy-induced hypertension* was defined as blood pressure of ≥140/90 mm Hg; *severe preeclampsia* was defined as diastolic blood pressure of ≥110 mm Hg and 0.3 g albumin/24 hours in the urine. We recorded the following parameters: gestational age at delivery, birthweight, birthweight percentile, and Apgar score <7 at 5 minutes. Parameters such as umbilical cord arterial pH, type of delivery (vaginal, emergency or planned cesarean section delivery), presence of respiratory distress, need of mechanical ventilation, and presence of a patent ductus arteriosus were also collected. The age at the first feeding, the type of feedings (maternal vs artificial milk), and use of intravenous feedings were also recorded. Hematocrit level and number of transfusions were noted.

Ethical considerations

After discussion with our institutional review board, specific ethics approval was judged unnecessary because sonographic measurements were performed as an integral part of routine clinical visits for which informed consent from patients was a part.

Statistical analysis

Descriptive statistics were presented as mean ± SDs for numeric variables and as percentages for categoric variables. The value of isthmic blood flow index and isthmic diastolic blood flow was converted into Z scores that were based on normal reference values from our unit. As a first step, the levels of significance of bivariate associations between pre- and postnatal variables and the development of NEC were assessed with the use of either