Original Article

Ductus venosus Doppler and the postnatal outcomes of growth restricted fetuses with absent end-diastolic blood flow in the umbilical arteries

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A B S T R A C T

Objective: We aimed to evaluate the outcomes of growth-restricted fetuses with absent end-diastolic velocity in the umbilical arteries (UA-AEDV), and investigate the relationship between Doppler flow velocity waveforms in the ductus venosus (DV) and the clinical features.

Materials and methods: This was a retrospective study of growth-restricted fetuses diagnosed with UA-AEDV delivered at our institution between 2013 and 2015. The time from diagnosis of UA-AEDV to delivery, postnatal survival, and developmental prognoses were the primary outcomes. The time lag between the occurrence of UA-AEDV and an abnormal increase in the DV pulsatility index (DV-PI) were investigated. We also examined the correlation between the DV-PI values immediately before birth and umbilical cord arterial pH at birth.

Results: The median gestational age at birth among the 18 subjects was 28 \pm 2 (24-34) weeks, and the observation period between the last measured DV-PI. A positive correlation (correlation coefficient, 0.68) was observed between the umbilical artery pH and the last measured DV-PI.

Conclusion: The time interval from initial detection of UA-AEDV to delivery is highly variable, and it is reasonable to manage these growth-restricted fetuses with UA-AEDV expectantly with careful surveillance for fetal well-being. Specifically, Doppler DV analysis is clinically valuable for their evaluation.

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Introduction

Early-onset of fetal growth restriction (FGR) remains one of the most challenging issues in obstetrics and is a leading cause of perinatal morbidity and mortality. Fetal Doppler is a widely used method for evaluating FGR. Among a few parameters, Doppler velocimetry of the umbilical artery (UA) provides important information on placental function. Placental dysfunction is associated with a rise in UA vascular resistance with a progressive decrease in the diastolic phase. This change exposes the fetus to hypoxic conditions leading to life-threatening hemodynamic changes. In severe cases, UA end-diastolic flow ceases and ultimately reverses, conditions known as absent end-diastolic velocity (UA-AEDV) and reverse end-diastolic velocity (UA-REDV), respectively. Affected fetuses are at risk for acidosis, hypoxemia, perinatal mortality, and serious morbidity [1–5]. There is no in utero therapy that can effectively reverse placental insufficiency; therefore, when UA-AEDV occurs prenatally, prompt delivery may be considered [6]. However, the optimal timing of delivery in the presence of UA-AEDV is debatable. Many previous investigators have emphasized the substantial impact of gestational age at delivery, on neonatal mortality and morbidity rates in FGR [7–10]. For this reason, it is desirable that delivery is postponed as long as possible to minimize the risks of prematurity and organ injury.

Meanwhile, Doppler examination of the ductus venosus (DV) flow velocity waveform has been widely used for fetal surveillance. In clinical practice, the observation of increased pulsatility due to decreased velocity during atrial contraction (a-wave) can be considered a sign of fetal compromise [11,12].
investigation of the longitudinal changes in vascular Doppler parameters described the typical progression pattern in FGR as an increased UA pulsatility index (PI), UA-AEDV followed by UA-REDV, an elevated DV-PI, and a reverse DV a-wave [13]. In this study, we aimed to investigate the perinatal and postnatal outcomes of severely growth-restricted fetuses with UA-AEDV, and the relationship between Doppler flow velocity waveforms in DV and the clinical features of these fetuses.

Materials and methods

Patients

We performed a chart review of patients diagnosed with FGR and UA-AEDV, managed at our institution between 2013 and 2015. The Kyushu University Hospital Ethical Review Board approved the study (Approval number 28-9). The US-estimated fetal body weight (BW, grams) was derived using an established formula for Japanese fetuses. The formula was based on biparietal diameter (BPD, cm), abdominal circumference (AC, cm), and femur length (FL, cm) and was defined as follows: \( BW = (1.07 \times BPD^{3}) + (0.30 \times AC^{2} \times FL) \) [14]. A fetus was defined as growth-restricted when the z-score of estimated weight was equal to or less than \(-1.5\) standard deviation (SD) of the Japanese standard. Cases presenting with structural or chromosomal abnormalities and multiple fetuses were excluded from the study.

Ultrasound examination

After the initial diagnosis of FGR, all patients underwent serial fetal ultrasound examination throughout their pregnancy. Doppler velocimetry was performed by experienced obstetricians with a Voluson E8 ultrasound system (GE Healthcare, Little Chalfont, UK). Flow velocity waveforms were obtained from the UA, middle cerebral artery (MCA), and DV. UA blood flow velocity waveforms were obtained from a free-floating loop of the umbilical cord. The angle of insonation was maintained as close to 0° as possible. Doppler velocimetry readings were accepted for analysis only after a clear, steady state was obtained. The presence of UA-AEDV or UA-REDV (UA-AEDV) was identified based on the visual evaluation of the blood velocity curve. In addition, blood flow signals of the DV were depicted in a mid-sagittal longitudinal plane of the fetal trunk using color Doppler. The angle between the ultrasound beam and the direction of the blood flow was maintained lower than 30°. The sample volume was limited to the isthmic portion of DV to avoid interference from blood flow in the inferior vena cava. A minimum of 5–10 successive waveforms were recorded and evaluated. The PI was calculated automatically by the machines using the following formula: \( PI = (Vs – Va)/Vmean \), where \( Vs = \) peak velocity during ventricular systole, \( Va = \) minimum velocity during atrial contraction and \( Vmean = \) mean velocity during the cardiac cycle. An elevation in the DV-PI greater than 90th percentile of the Japanese standard was considered abnormal [15]. Concurrently, Doppler measurements were obtained from the MCA. The MCA resistance index (MRA-RI) was measured in an axial section of the fetal brain at the level of cavum septi pellucidi and thalamus.

Institutional management policy for preterm fetal growth restriction

Upon admission to our hospital for FGR, fetal well-being was assessed daily using cardiotocogram and ultrasonography. Fetal indications for emergent cesarean delivery included a non-reassuring pattern during non-stress test (NST) (recurrent severe variable decelerations, late decelerations, prolonged decelerations, and variability loss) and a low biophysical profiling score (BPS). When a reversed a-wave was found in the DV, prompt cesarean delivery was also indicated. UA-AREDV alone was not considered an indication for delivery. Interpretation of a low BPS was based on the established policy provided by Manning [16]; that is, a BPS of 6 in the presence of oligohydramnios (amniotic fluid pocket less than 2 cm), or scores of 4, 2 and 0 were considered as indications for emergent cesarean delivery if the gestational age was \( \geq 32 \) weeks. A BPP of 4 in the presence of oligohydramnios or scores of 2 and 0 were considered indications for emergent cesarean delivery if the gestational age was \( \geq 26 \) weeks. Blood gas was sampled from an umbilical cord segment clamped immediately after birth. Following delivery, neonatal care was assumed by an expert neonatology team.

Following discharge from the neonatal intensive care unit, neonates underwent follow-up examinations and developmental assessment using the Kyoto Scale of Psychological Development. This test is a standardized face-to-face instrument that is widely used in Japanese clinical settings to measure an individual’s development in three areas, i.e., Postural-Motor, Cognitive-Adaptive, and Language—Social, providing an overall Developmental Quotient (DQ) and a DQ for each area [17,18]. A poor postnatal outcome was defined as postnatal death or a major developmental disability. A major developmental disability was defined as cerebral palsy (CP), intellectual disability (ID), and/or epilepsy. The diagnosis of CP was based on typical motor findings with or without additional signs of cognitive delay. ID was defined as an overall DQ of less than 70.

Study design

The time from diagnosis of UA-AEDV to delivery, gestational age at delivery, postnatal life prognoses, and major developmental disabilities were considered the primary outcomes for this study. The medical charts were reviewed and, in addition to the above data, the following information was recorded: gestational age at diagnosis of UA-AEDV, abnormally elevated DV-PI, progression to UA-REDV or reversed DV a-wave, the UA-RI, MCA-RI, and DV-PI immediately before delivery, the indications for delivery, and umbilical cord arterial pH at birth. These findings in the favorable outcomes group were compared to those in the poor outcomes group.

Next, we investigated the relationship between the DV waveform abnormalities and clinical features. Specifically, we determined the time from occurrence of UA-AEDV to the development of an elevated DV-PI and assessed the association of this period with the postnatal outcome. Further, we examined the correlations of DV-PI and MCA-RI values immediately before birth with the umbilical cord arterial pH at birth.

Statistical analysis

Data is reported as median with range when data is not normally distributed. Intergroup comparisons were performed using the chi-square and Mann–Whitney test for categorical and continuous outcomes, respectively. Correlations were analyzed using Spearman’s correlation coefficient. A P value of less than 0.05 was considered statistically significant. Statistical analysis was performed using the SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA).

Results

Twenty patients with FGR and UA-AEDV were encountered. Two fetuses died in utero, and these cases were omitted from our study because the cause of death was extremely low birth weight (230 g
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