

Doppler assessment between pathological examination of the placenta and late fetal intrauterine demise

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Summary

Aim: The relation between placental histopathological examination, umbilical cord pathology and abnormal umbilical and cerebral Doppler as a predictor of stillbirth at later gestations was evaluated. **Materials and Methods:** A retrospective study of 55 monofetal pregnancies complicated with late fetal death from 2005-2008 was conducted at the Institute of Gynecology and Obstetrics, Belgrade. Statistical analysis: chi-square likelihood ratio test and Spearman's coefficient correlation. **Results:** Intrauterine fetal demise occurred most frequently at term –32.7% of the time. Changes in the umbilical artery resistance index were not significantly different from placental histopathology findings, $p = 0.363$. There was a significant correlation between neonatal birth weight and weeks of gestation at delivery, $r = 0.796$; $p = 0.001$. **Conclusion:** Umbilical artery Doppler is a relatively poor predictor of stillbirths due to placental dysfunction. It seems that neonatal birth weight is the best predictor of late stillbirth in high-risk pregnancies.

Key words: Doppler; Fetus; Umbilical and cerebral velocimetry; Placenta; Umbilical cord; Fetal demise.

Introduction

The World Health Organization (WHO) defines stillbirth as “fetal death late in pregnancy” and allows each country to define the gestational age at which fetal death is considered a stillbirth for reporting purposes [1]. As a result, some countries (Serbia) define stillbirth as early as 16 weeks of gestation, whereas others use a threshold as late as 28 weeks. This stratification allows for a relatively reliable international comparison of late fetal losses, and enables division of stillbirths into those that are more difficult to prevent (early losses) from losses that might potentially be preventable (late losses) [2]. In 2008, stillbirths occurred in 0.9% of late pregnancies, at or after 28 weeks of gestation, at the Institute of Gynecology and Obstetrics, Belgrade.

Indications for pathologic examination include poor pregnancy outcome (prematurity, IUGR, perinatal death, asphyxia), systemic maternal disorders, third-trimester bleeding and evidence of fetal or maternal infection [3].

In pregnancies complicated by placental dysfunction, there may be a reduction in the number of functional villi and/or small blood vessels with resulting increased impedance, mainly reflected by decrease in end-diastolic velocity. When the resistance increases even more, there is no diastolic forward velocity (absent end-diastolic velocity - AEDV). Further increase in the resistance causes reversed end-diastolic velocity-REDV and middle cerebral centralization, a late step in the cascade of events leading to intrauterine fetal demise [4].

The aim of the study was to assess the accuracy of pathological antepartum Doppler velocimetry AEDV, REDV and the middle cerebral artery centralization on prediction of the intrauterine fetal demise. The difference between placental histopathology examination, umbilical cord pathology and abnormal umbilical and cerebral Doppler as a predictor of stillbirth at later gestations was also evaluated.

Materials and Methods

Fifty-five pregnancies at and after the 28th gestational week complicated with intrauterine fetal death, and treated at the Institute of Gynecology and Obstetrics, Clinical Center of Serbia from 2005 to 2008 were retrospectively included in the study. Gestational age was calculated according to date of the last menstrual period and confirmed by first trimester ultrasonography. If there was a discrepancy (more than five days), ultrasound examination was used to determine gestational age.

Intrauterine fetal death was based on: 1) Cessation of fetal movements –50.0% (25/55), 2) Absence of fetal heart tones CTG –54.5% (30/55), and, 3) Absence of fetal cardiac activity observed by real-time ultrasound –100.0%.

Fetal weight was estimated using Hadlock's method based on measurements of the fetal head, body and femur. The fetal biophysical profile was performed for 20 min every day [5]. The last Doppler examination was performed approximately two days before intrauterine fetal demise diagnosed in 49 controlled pregnancies. We did not perform a fetal biophysical profile nor Doppler examination of fetoplacental circulation in six non-controlled pregnancies. A combined real time pulsed Doppler system fitted with a 3.75 MHz curvilinear probe (TOSHIBA) was used. The spatial peak temporal average power did not exceed 87 mW/cm. The Doppler angle of insonation was less than 30, the sweep speed was 2.5 cm/s and the pulse repetition frequency ranged from 3.5 KHz to 5.0 KHz. The women rested

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in a semi-recumbent position during Doppler examination. All measurements were performed by the same physician during fetal apnea. Blood velocity waveforms were obtained from both the umbilical and fetal middle cerebral arteries. The umbilical artery was insonated close to its placental insertions and the middle cerebral artery about 1 cm distal to its origin from the internal carotid artery. The resistance index was calculated for each vessel by averaging the first two good quality resistance indexes obtained from two consecutive waveforms.

Placentas were collected at delivery and fixed in 10% formalin for three to four days. After removal of the membranes and umbilical cord, placental weight was recorded. Gross and microscopic studies of the placentas were performed according to established pathologic protocols.

Multifetal pregnancies, suspected fetal congenital malformations and maternal Rh isoimmunization were excluded from the study.

Continuous variables were presented as mean (standard deviation as 95% confidence interval) assessed for normality or not, and comparisons were made using the chi-square likelihood ratio test to estimate the difference between resistance indexes in umbilical artery (UA RI), middle cerebral artery (MCA RI) and placental histopathology examination as well as umbilical cord pathology. Spearman's correlation test was used to estimate significance of correlation between neonatal birth weight and weeks of gestation at delivery.

Results

The mean age of all women participating in our study was 29.39 ± 6.53 years. Of the women, 21.8% were older than 35 years. Most of them were nulliparas –71% and educated –78.2%. Recurrent intrauterine fetal demise was found in two cases. The majority of women had adequate prenatal care in their pregnancy (89.1%), but 11.1% were non-controlled. The most common cause of fetal death may be attributable to pregnancy-induced hypertension, accounting for 23.6% (13/55), and preeclampsia –11.0% (6/55). Intrauterine growth restriction was diagnosed in 52.7% of (29/55) fetuses.

Biophysical profile (BPP) score was 6 in six (12.2%) while BPP score was 4 in 35 (71.4%) fetuses. In eight fetuses the BPP score was 2.

Eight fetuses had an increased resistance index in UA, but 27 fetuses had no structural or chromosomal abnormalities in which the development of AEDV was evidenced by Doppler imaging. RDEV was diagnosed in six and cerebral centralization in eight fetuses. In our study, the time interval between the incidence of AEDV in the umbilical artery and fetal death was 48 hours as documented by placental findings, and there were no documented normal Doppler findings in pregnancies complicated with fetal demise.

The most common placental histopathology findings were infarct in 46.5% and chorioamnionitis in 23.3% of cases. Changes in the umbilical artery resistance index (AU RI) were not significantly different from placental histopathology findings ($p = 0.363$). There were no measured changes of umbilical artery resistance indexes in 11.0% (6/55) as well as no documented histopathological findings of placenta in 3.6% (2/55) of fetuses.

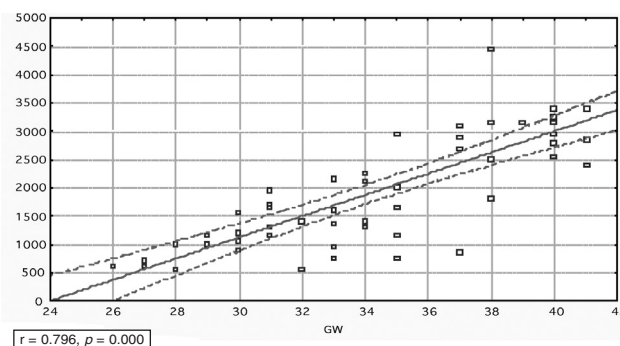


Figure 1. — Neonatal birthweight significantly correlated with gestational age at delivery ($r = 0.796$; $p = 0.000$; Spearman's Rho test).

The most common umbilical cord pathology associated with fetal demise was short cord in 16 (29.1%), cord compression in 14 (25.5%), long cord in seven (12.7%) and true knot in six (10.9%) cases. We documented normal findings of the umbilical cord in 12 (21.8%) cases. There was no significant difference between abnormal Doppler velocity and long cord ($p = 0.572$), short cord ($p = 0.699$) and true knot ($p = 0.999$).

Intrauterine fetal demise occurred most frequently at term in 38.2% of cases and from 29 to 32 weeks in 27.3%.

Labor should be induced as soon as possible after diagnosis, and in our study the time was approximately four hours.

Mean neonatal weight was 1927.27 ± 1011.84 g (median 1650; IQR 1700). A large number of fetuses, i.e., 34.5%, weighed over 2,500 g. There was a significant correlation between neonatal birth weight and weeks of gestation at delivery $r = 0.796$; $p = 0.000$ (Figure 1).

Discussion

Fetal death of unknown cause is a special problem. Maternal studies that are to be considered during analysis of fetal demise should include advanced maternal age. In our study, 78.2% of patients were younger than 35 years and the majority were educated nulliparas [6]. Our study showed that maternal hypertension was the most frequent complication of pregnancies. Up to 60% of stillbirths have no identifiable etiology. Attempting to identify the cause of fetal death is important because it may have an influence on estimate of recurrence and future pre-conceptional counseling, pregnancy management, prenatal diagnostic procedures and neonatal management [7]. The majority of women, 89.1%, had adequate prenatal care in pregnancy.

BPP scores were low in most of the high-risk pregnancies. Decrease in amniotic fluid index is long-term effects of chronic fetal hypoxia. Changes in the fetal heart rate are the first reactions to hypoxia regardless of the etiology [8].

The combination of small abdominal circumference, normal anatomy, low BPP score values and abnormal

umbilical artery Doppler recording is strongly suggestive of fetal IUGR due to placental insufficiency, i.e., in 52.7% of cases. Doppler may distinguish between small normal fetuses that will not manifest any abnormal placental vasculature and fetuses affected by conditions causing restricted growth, secondary to a placental condition (such as preeclampsia) and who are, thus, at higher risk of intrapartum difficulties and perinatal mortality [9]. In fetuses at risk of intrauterine demise, changes in Doppler characteristics of various vascular beds may reflect progressive worsening of placental dysfunction. Kurkinen-Rati *et al.* [10] concluded in their study that early AEDV or REDV (before 34 gestational weeks) in the umbilical artery was a serious warning signal of probable fetal distress. In such case, the rates of perinatal morbidity and mortality are very high, which is a reflection of the severity of the condition. Twenty-seven fetuses had no structural and chromosomal abnormalities in which the development of AEDV was evidenced by Doppler imaging. Sallout *et al.* evaluated the time interval between incidence of AEDV in the umbilical artery and either the development of abnormal fetal heart-rate patterns or delivery [11]. In our study, this time interval was approximately 48 hours.

There was almost an insignificant difference between changes in UA RI and placental histopathology findings. Our study showed that umbilical artery Doppler recording was a relatively poor predictor of stillbirths due to placental dysfunction. We did not diagnose normal Doppler findings in umbilical and cerebral circulation in pregnancies complicated of fetal demise. The umbilical cord pathology was not associated with fetal demise. In six cases, true knot was not diagnosed by ultrasound examination.

Abnormal Doppler velocity was not associated with umbilical cord pathology. The association is highest in stillbirths due to umbilical cord lesions, occurring at 29 to 32 weeks as well as at term.

When a dead fetus is left in the uterus for three to four weeks (in our study it was approximately 48 hours), fibrinogen levels may drop, leading to coagulopathy [12].

Almost one-third of neonates weighed over 2,500 g. Resnik and Creasy [5] reported that birthweight after 29 weeks appeared to be a better predictor of survival than gestational age, as documented in our study as well (Figure 1).

Conclusion

Weekly biophysical profile or fetal heart rate testing can be combined with maternal kick counts in the third trimester. Umbilical artery Doppler is relatively poor predictor of stillbirths due to placental dysfunction. It seems that neonatal birth weight is the best predictor of late stillbirth in high-risk pregnancies.

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