OBSTETRICS

Discordance in fetal biometry and Doppler are independent predictors of the risk of perinatal loss in twin pregnancies

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OBJECTIVE: Impaired fetal growth might be better evaluated in twin pregnancies by assessing the intertwin discordance rather than the individual fetal size. The aim of this study was to investigate the prediction of perinatal loss in twin pregnancy using discordance in fetal biometry and Doppler.

STUDY DESIGN: This was a retrospective cohort study in a tertiary referral center. The estimated fetal weight (EFW), umbilical artery (UA) pulsatility index (PI), middle cerebral artery (MCA) PI, cerebroplacental ratio (CPR), and their discordance recorded at the last ultrasound assessment before delivery or demise of one or both fetuses were converted into centiles or multiples of the median (MoM). The discordance was calculated as the larger value—smaller value/larger value. A logistic regression analysis was performed to identify, and adjust for, potential confounders. The predictive accuracy was assessed using receiver-operating characteristic curve analysis.

RESULTS: The analysis included 620 (464 dichorionic diamniotic and 156 monochorionic diamniotic) twin pregnancies (1240 fetuses). Perinatal loss of one or both fetuses complicated 16 pregnancies (2.6%). The combination of EFW discordance and CPR discordance had the best predictive performance (area under the curve, 0.96; 95%

confidence interval, 0.92—1.00) for perinatal mortality. The detection rate, false-positive rate, positive likelihood ratio, and negative likelihood ratio were 87.5%, 6.7%, 13.08, and 0.13, respectively. The EFW centile, EFW below the 10th centile (small for gestational age), UA PI discordance, MCA PI discordance, and MCA PI MoM were significantly associated with the risk of perinatal loss on univariate analysis, but these associations became nonsignificant after adjusting for other confounders ($P = .097$, $P = .090$, $P = .687$, $P = .360$, and $P = .074$, respectively). The UA PI MoM, CPR MoM, EFW discordance, and CPR discordance were all independent predictors of the risk of perinatal loss, even after adjusting for potential confounders ($P = .022$, $P = .002$, $P < .001$, and $P = .010$, respectively).

CONCLUSION: EFW discordance and CPR discordance are independent predictors of the risk of perinatal loss in twin pregnancies. Their combination could identify the majority of twin pregnancies at risk of perinatal loss. These findings highlight the importance of discordance in Doppler indices of fetal hypoxia, as well as fetal size, in assessing the risk of perinatal mortality.

Key words: cerebroplacental ratio, estimated fetal weight, impaired fetal growth, twin pregnancies, intertwin discordance

T win pregnancy is associated with an increased risk of perinatal mortality and morbidity; the risk is significantly higher in monochorionic compared

with dichorionic pregnancies.[1-4] In 2009, the stillbirth rate in the United Kingdom was 12.3 per 1000 twin births, compared with 5 per 1000 singleton births.[5]

The incidence of twins is rising, mainly because of assisted reproduction techniques.[6] In 1980, 10 women per 1000 giving birth in England and Wales had multiple births compared with 16 women per 1000 in 2009.[5] Ultrasound assessment of fetal biometry is used to identify and monitor twin pregnancies at risk of adverse pregnancy outcome, such as selective fetal growth restriction (sFGR). In a singleton pregnancy, impaired fetal growth can be assessed by comparing biometry and Doppler indices against

standards for uncomplicated pregnancies. However, this might be better evaluated in twin pregnancies by assessing the intertwin discordance.[3,7]

Both birthweight and estimated fetal weight (EFW) discordance have been shown to be strongly associated with adverse pregnancy outcome.[3,8] The UK National Institute for Health and Care Excellence guidelines for the clinical management of multiple pregnancy state that a 25% or greater difference in size between twins should be considered an important clinical indicator of fetal growth restriction (FGR) and that this finding should trigger referral to a tertiary level fetal medicine center.[6] Similarly, the American College of Obstetricians and

TABLE 1

Comparison of the study population groups according to the outcome of pregnancies

Variable	Pregnancies without perinatal loss (n = 604)	Pregnancies complicated by perinatal loss (n = 16)	P value
Maternal age in years, median (IQR)	33.00 (30.00—36.00)	32.50 (29.25—35.75)	.463
Body mass index (kg/m^2), median (IQR)	24.30 (21.50—27.40)	24.30 (22.40—25.60)	.91
Nulliparous, n (%)	359 (59.4)	8 (50.0)	.448
Ethnicity, n (%)			.870
Caucasian	458 (75.8)	11 (68.8)	
African	64 (10.6)	3 (18.8)	
Asian	75 (12.4)	2 (12.5)	
Mixed	3 (0.5)	0	
Other	4 (0.6)	0	
Smoker, n (%)	22 (3.6)	1 (6.3)	.586
Assisted conception, n (%)	150 (25.0)	2 (13.03)	.299
Monochorionicity, n (%)	152 (25.2)	4 (25.0)	.988
Gestational age at ultrasound (wks), median (IQR)	34.57 (33.00—35.57)	27.43 (23.65—29.00)	< .001
Gestational age at delivery (wks), median (IQR)	37.00 (35.29—37.43)	31.50 (26.15—33.46)	< .001
Estimated fetal weight discordance	8.31 (4.03—15.69)	36.12 (20.49—50.96)	< .001
Umbilical artery pulsatility index discordance	13.54 (6.74—26.36)	25.58 (7.65—50.78)	.074
Middle cerebral artery pulsatility index discordance	13.08 (5.88—23.06)	23.38 (14.91—31.88)	.003
Cerebroplacental ratio discordance	17.43 (8.65—30.54)	44.26 (26.59—68.33)	< .001

IQR, interquartile range.

Khalil. Cerebroplacental Ratio in twin pregnancies. Am J Obstet Gynecol 2015.

Gynecologists considers 15—25% EFW discordance as a cutoff for the diagnosis of significantly discordant fetal growth.[9]

The ratio of middle cerebral to umbilical artery Doppler indices, also termed the cerebroplacental ratio (CPR), has an established role in predicting adverse outcome in singleton pregnancies complicated by small for gestational age.[10,11] Recently assessment of CPR has also been shown to be of value in assessing average for gestational age fetuses that are compromised by placental insufficiency at term.[12,13]

CPR is emerging as a better proxy marker of fetal compromise, in particular secondary to placental insufficiency and hypoxemia, than fetal size alone.[12-16] Despite the fact that CPR has been investigated in many studies in singleton pregnancies, there is a paucity of data on the value of CPR in predicting adverse outcome in twin pregnancy. There is limited evidence suggesting that the value of CPR in twin pregnancies could be similar to that reported in singleton pregnancies.[17] Gaziano et al[17] have demonstrated that CPR has been shown to be

superior to umbilical artery (UA) and middle cerebral artery (MCA) in predicting adverse fetal and neonatal outcomes, such as growth restriction and the length of stay in the neonatal unit.

The main aim of this study was to investigate the role of fetal size, Doppler indices, and their discordance in the prediction of perinatal loss in twin pregnancies.

MATERIALS AND METHODS

This was a retrospective cohort study in a single tertiary referral center over a 14 year period from 2000 to 2013. Cases were identified by searching the ViewPoint database (ViewPoint 5.6.8.428; ViewPoint Bildverarbeitung GmbH, Weßling, Germany) in the fetal medicine unit (St George's Hospital). The inclusion criteria were twin pregnancies in which routine fetal biometry, UA, and MCA Doppler were recorded at the last visit before delivery or the diagnosis of intrauterine death of one or both fetuses. Gestational age (GA) was determined by the crown-rump length of the larger twin at the 11-14 week scan or by head circumference if assessed after 14 weeks' gestation.[18,19]

Chorionicity was determined by ultrasound evaluation according to the number of placentas and the presence of the lambda or T signs, and confirmed after birth.[20] Pregnancies complicated by structural or chromosomal abnormalities, twin to twin transfusion syndrome, twin reversed arterial perfusion, of unknown chorionicity, monochorionic monoamniotic, and high-order multiple gestations were not included in the analysis. Pregnancies ending in termination or loss to follow-up were also excluded.

The main outcome in this study was perinatal loss. Stillbirth was defined as the death of the fetus after 24 weeks and before birth, whereas perinatal loss included stillbirth and neonatal death within the first 28 days. The study was exempt from review by the Wandsworth Research Ethics Committee. There was an overlap between the population of this study and that of the Southwest Thames Obstetric Research Collaborative (STORK) cohort.[3] However, the STORK cohort included 9 hospitals, the period