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# Birth-weight discordance and neonatal morbidity in twin pregnancy: analysis of STORK multiple pregnancy cohort

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**KEYWORDS:** morbidity; outcome; twin pregnancy; weight discordance

## ABSTRACT

***Objectives*** *To investigate the relationship between weight discordance and neonatal morbidity in twin pregnancy progressing to at least 34 weeks of gestation. The secondary aim was to determine the predictive accuracy of different weight discordance cut-offs in predicting neonatal morbidity in twin pregnancy.*

***Methods*** *This was a retrospective multicenter cohort study of all twin pregnancies booked for antenatal care at four hospitals in the Southwest Thames region of London Obstetric Research Collaborative (STORK) over a period of 10 years. Ultrasound data were obtained by a search of each hospital's obstetric ultrasound computer database, while outcome details were obtained from the computerized maternity and neonatal records. The primary outcome was incidence of composite neonatal morbidity in twin pregnancy with birth-weight discordance. Logistic regression was used to identify and adjust for potential confounders, while a receiver–operating characteristics (ROC) curve was used to determine predictive accuracy.*

***Results*** *Nine hundred and thirty-nine twin pregnancies (760 dichorionic, 179 monochorionic) were included. Gestational age at birth and birth-weight decile were significantly lower in pregnancies complicated by neonatal morbidity compared with those which were not ($P < 0.001$ for both). On multivariable logistic regression analysis, gestational age at birth ($P < 0.001$), birth-weight decile ($P = 0.029$) and birth-weight discordance ($P = 0.019$), but not chorionicity ($P = 0.477$) or presence of at least one small-for-gestational-age (SGA) twin ($P = 0.245$), were associated independently with the risk of neonatal morbidity. There was a progressive increase in the risk of neonatal morbidity with increasing birth-weight discordance. Despite this association, birth-weight discordance showed an overall poor predictive accuracy for neonatal morbidity, with an area under the ROC curve of 0.58 (95% CI, 0.53–0.63) with an optimal cut-off of 17.6%, showing sensitivity and specificity of 35.2% (95% CI, 27.8–43.2%) and 83.2% (95% CI, 80.4–85.8%), respectively.*

***Conclusion*** *Intertwin birth-weight discordance is associated independently with the risk of neonatal morbidity in twins born after 34 weeks' gestation, irrespective of chorionicity or diagnosis of SGA in either twin. However, its predictive accuracy for neonatal morbidity is poor. Copyright © 2017 ISUOG. Published by John Wiley & Sons Ltd.*

## INTRODUCTION

Birth-weight discordance is one of the major determinants of perinatal mortality in twin pregnancy, irrespective of chorionicity[1,2]. Although a certain degree of discordance in fetal growth is present invariably in all twin pregnancies, intertwin size discordance has been associated with a multitude of adverse outcomes including stillbirth, neonatal death, preterm birth, respiratory distress and admission to the neonatal intensive care unit (NICU)[2–20].

Despite the fact that the association between weight discordance and fetal loss is well established, there is still controversy regarding the actual role of discordant fetal growth in determining perinatal morbidity. The pathophysiology of fetal growth disorders in twin pregnancy has not yet been completely elucidated. The uterine milieu can meet the metabolic demands of both twins during the second and early third trimesters, until approximately 28–32 weeks, after which twin growth usually diverges from that of singletons[21,22]. A multitude of weight discordance cut-offs have been suggested to be associated with adverse pregnancy outcome, but it is yet

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to be established which one provides the best combination of sensitivity and specificity.

The primary aim of this study was to investigate the association between weight discordance and neonatal morbidity in twin pregnancy progressing to at least 34 weeks of gestation. The secondary aim was to determine the predictive accuracy of intertwin weight discordance for the risk of neonatal morbidity.

## METHODS

This was a retrospective cohort study of all twin pregnancies booked for antenatal care at four hospitals (St George's, Kingston, Epsom and St Helier Hospitals) in the Southwest Thames region of London Obstetric Research Collaborative (STORK) over a period of 10 years from 2000. Scan data were obtained by a search of each hospital's obstetric ultrasound computer database, while outcome details were obtained from maternity and neonatal records. These databases were crosschecked to ensure full data capture of all twin pregnancies during the study period. All data included in the analysis were collected prospectively but analyzed retrospectively. Terminations of pregnancy, fetal or chromosomal abnormalities, cases affected by twin to twin transfusion syndrome (TTTS), pregnancies of unknown chorionicity, monochorionic monoamniotic pregnancies, higher order multiple gestations, pregnancies complicated by stillbirth and those delivering before 34 weeks were not included in the analysis.

Gestational age was determined according to crown–rump length of the larger twin at the 11–14-week scan[23]. Chorionicity was determined by ultrasound evaluation according to the number of placentas and the presence of the lambda or T-sign, and was confirmed after birth[24]. A routine fetal structural survey was carried out at 18–22 weeks, and all monochorionic (MC) twins had two additional scans at around 17 and 19 weeks specifically to identify early features of TTTS. If TTTS was suspected, women were referred to the local tertiary center for assessment for fetoscopic laser ablation of the placental interconnecting vessels. Decisions regarding mode of delivery were made according to the individual patient's wishes and the attending obstetrician's own clinical practice. Delivery, whether by induction of labor or elective Cesarean section, was planned from 37 weeks' gestation in dichorionic (DC)–diamniotic twin pregnancies and from 36 weeks in monochorionic–diamniotic twin pregnancies.

The primary outcome was incidence of composite neonatal morbidity, defined as the occurrence of at least one of the following outcomes in either twin[25]: respiratory morbidity (including respiratory distress syndrome, transient tachypnea of the newborn, continuous positive airway pressure for at least 24 h, mechanical ventilation, need for supplemental oxygen, pulmonary hypertension or bronchopulmonary dysplasia); infectious morbidity (including pneumonia, meningitis and culture-proven sepsis); neurological morbidity (including seizures, intraventricular hemorrhage grade III or IV and periventricular leukomalacia grade II or III detected on ultrasound examination); hypoglycemia (blood glucose $< 2.2$ mmol/L); hypothermia (core body temperature $< 36.0\,^{\circ}$C); jaundice and need for phototherapy; necrotizing enterocolitis (any grade); or retinopathy of prematurity (any grade).

Birth-weight discordance was calculated as 100 × (birth weight of larger twin − birth weight of smaller twin)/birth weight of larger twin[1]. Pregnancies affected by single fetal loss or neonatal death were excluded from the analysis.

### Statistical analysis

Continuous variables are presented as median (interquartile range), while categorical variables are presented as *n* (%). The distribution assumptions were tested using the Shapiro–Wilk test. Group comparison of the variables was performed using Student's *t*-test, the Mann Whitney *U*-test or the chi-square test where appropriate. We first examined potential difference in the incidence of neonatal morbidity according to intertwin birth-weight discordance. We also examined potential confounders, such as chorionicity, gestational age at birth, birth-weight decile of each twin (calculated according to published reference ranges in twin pregnancies), presence of one or more small-for-gestational age (SGA) (defined as birth weight $< 10^{th}$ centile) twin[26]. The potential associations between these parameters and the risk of neonatal morbidity were evaluated initially using univariable regression analysis.

Potential independent predictors of risk of neonatal morbidity (monochorionic pregnancy, gestational age at birth, birth weight, birth-weight discordance and SGA status) were then evaluated using binary logistic regression. All covariates were included *a priori* in the final model. Goodness-of-fit was checked using the Hosmer–Lemeshow test, and predictive accuracy was assessed using C-statistics (area under the receiver–operating characteristics curve; AUC). Standard postestimation tests were used to check the final model's validity, performing multicollinearity and influential observation analyses (using standardized residuals, change in Pearson's *r* and deviance chi-square). There were no missing values, and thus no imputation technique was adopted.

Finally, we assessed the predictive accuracy of birth-weight discordance for the risk of neonatal morbidity using summary estimates of sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, and positive (LR+) and negative (LR−) likelihood ratios, and used diagnostic odds ratios for various cut-offs of birth-weight discordance[27].

Statistical significance was defined as a two-sided $P$-value $< 0.05$, and all analyses were carried out using Stata version 13.1 (Stata Corp., College Station, TX, USA, 2013) and SPSS Statistics version 24 (IBM Corp., Armonk, NY, USA).

## RESULTS

The study included 950 twin pregnancies (768 DC, 182 MC) that delivered from 34 weeks of gestation. After exclusion of seven fetuses that experienced intrauterine death (four DC and three MC) and four neonatal deaths (one early and three late, all occurring in DC pregnancies), 939 twin pregnancies (760 DC, 179 MC) were available for analysis. There was no case of cotwin demise after the death of a fetus if it occurred from 34 weeks of gestation. The characteristics of the population analyzed in the present study are shown in Table 1. The incidence of composite neonatal morbidity in this cohort of twin pregnancies was 16.9% (95% CI, 14.6–19.5) (Table S1).

Gestational age at birth and median birth-weight decile were significantly lower in pregnancies complicated by neonatal morbidity compared with those that were not ($P < 0.001$ for both). When compared with pregnancies unaffected by neonatal morbidity, median birth weight, of either the larger or the smaller twin, was significantly lower in pregnancies complicated by neonatal morbidity ($P < 0.001$ for both; Table 1). Birth-weight discordance was significantly higher in affected (10.9, IQR 4.7–20.7) compared with in unaffected (8.7, IQR 4.0–14.6) twins ($P = 0.002$). There was no significant difference in the proportion of pregnancies with birth-weight discordance ≥ 5% ($P = 0.692$) or ≥ 10% ($P = 0.128$) between those complicated by neonatal morbidity and those that were not, while birth-weight discordances ≥ 15%, ≥ 20%, ≥ 25% and ≥ 30% were significantly more common in pregnancies affected by neonatal morbidity compared with those that were not ($P < 0.001$ for all; Table 1). The prevalence of at least one twin affected by SGA was significantly higher in the group affected by neonatal morbidity ($P < 0.001$; Table 1).

On multivariable logistic regression analysis, gestational age at birth (odds ratio (OR), 0.43; 95% CI, 0.37–0.50; $P < 0.001$), birth-weight decile (OR, 0.90; 95% CI, 0.81–0.99; $P = 0.029$) and birth-weight discordance (OR, 1.03; 95% CI, 1.01–1.05; $P = 0.019$), but not chorionicity ($P = 0.477$) or presence of at least one SGA twin ($P = 0.245$), were associated independently with risk of neonatal morbidity (Table 2). Likewise, gestational age at birth (OR, 0.42; 95% CI, 0.36–0.49; $P < 0.001$), birth-weight decile (OR, 0.86; 95% CI, 0.79–0.95; $P = 0.003$) and birth-weight discordance (OR, 1.03; 95% CI, 1.01–1.05; $P = 0.018$), but not chorionicity ($P = 0.314$) or presence of at least one SGA twin ($P = 0.107$), were associated independently with risk of admission to NICU (Table 2).

Risk of neonatal morbidity was then assessed according to the most commonly reported intertwin birth-weight discordance cut-offs (Table 3). When considering a threshold of 20%, in twins affected compared with those unaffected by intertwin birth-weight discordance, rates of neonatal morbidity (30.7% *vs* 14.5%, $P < 0.001$)

**Table 1** Characteristics of study cohort of twin pregnancies that delivered ≥ 34 weeks' gestation, overall and compared between those affected and those unaffected by neonatal morbidity

| *Characteristic* | *Overall (n = 939)* | *Neonatal morbidity* (n = 159)* | *No neonatal morbidity (n = 780)* | P |
|---|---|---|---|---|
| Monochorionic | 179 (19.1) | 31 (19.5) | 148 (19.0) | 0.876† |
| Gestational age at birth (weeks) | 36.7 ± 1.3 | 35.5 ± 1.3 | 36.9 ± 1.2 | < 0.001‡ |
| Birth weight (g) | | | | |
| Overall | 2572.5 (2323.8–2824.5) | 2267.5 (2005.8–2550.5) | 2625.5 (2397.5–2860.0) | < 0.001§ |
| Larger twin | 2700.0 (2460.0–2980.0) | 2440.0 (2197.5–2705.0) | 2750.0 (2520.0–3021.5) | < 0.001§ |
| Smaller twin | 2440.0 (2175.5–2679.0) | 2120.0 (1777.5–2402.5) | 2482.5 (2332.0–2711.5) | < 0.001§ |
| Birth-weight decile | | | | |
| Overall | 4.53 (2.5–6.5) | 3.05 (1.4–6.1) | 4.81 (2.8–6.6) | < 0.001§ |
| Larger twin | 5.07 (3.2–7.2) | 3.99 (2.3–6.8) | 5.36 (3.4–7.3) | < 0.001§ |
| Smaller twin | 3.88 (1.8–6.0) | 2.25 (0.5–4.9) | 4.07 (2.2–6.1) | < 0.001§ |
| Birth-weight discordance (%) | 9.0 (4.2–15.4) | 10.9 (4.7–20.7) | 8.7 (4.0–14.6) | 0.002§ |
| Birth-weight discordance: | | | | |
| ≥ 5% | 644 (68.6) | 114 (71.7) | 530 (67.9) | 0.692† |
| ≥ 10% | 424 (45.2) | 81 (50.9) | 343 (44.0) | 0.128† |
| ≥ 15% | 246 (26.2) | 60 (37.7) | 186 (23.8) | < 0.001† |
| ≥ 20% | 140 (14.9) | 43 (27.0) | 97 (12.4) | < 0.001† |
| ≥ 25% | 71 (7.6) | 28 (17.6) | 43 (5.5) | < 0.001† |
| ≥ 30% | 31 (3.3) | 15 (9.4) | 16 (2.1) | < 0.001† |
| SGA affecting one or both twins | 421 (44.8) | 95 (59.7) | 326 (42.0) | < 0.001† |
| Admission to NICU | 187 (19.9) | 156 (98.1) | 31 (4.0) | < 0.001† |

Data are given as *n* (%), mean ± SD or median (interquartile range). *Composite outcome of respiratory morbidity, infectious morbidity, neurological morbidity, hypoglycemia, hypothermia, jaundice, need for phototherapy, necrotizing enterocolitis and retinopathy of prematurity. †Chi-square test. ‡*t*-test. §Mann–Whitney *U*-test. NICU, neonatal intensive care unit; SGA, small-for-gestational age.

 

and admission to NICU (35.7% *vs* 17.1%, $P < 0.001$) were significantly higher, while gestational age at birth (36.4 ± 1.3 *vs* 36.7 ± 1.3, $P = 0.011$) was significantly lower. Likewise, in twins affected compared with those unaffected by intertwin birth-weight discordance of 25%, rate of neonatal morbidity (39.4% *vs* 15.1%, $P < 0.001$) and rate of admission to NICU (43.7% *vs* 18.0%, $P < 0.001$), but not gestational age at birth ($P = 0.062$), were significantly higher. Pregnancies were complicated by neonatal morbidity of both twins in 44.7% (95% CI, 36.8–52.7%; 71/159) of cases. Rate of neonatal morbidity was significantly higher in the smaller compared with in the larger twin, both in the overall population and in DC pregnancies ($P < 0.001$), while there was no difference in MC pregnancies ($P = 0.772$).

There was a progressive increase in the risk of neonatal morbidity with increasing birth-weight discordance cut-offs (Table 4). Despite this association, intertwin birth-weight discordance showed an overall poor predictive accuracy for neonatal morbidity, with an AUC of 0.58 (95% CI, 0.53–0.63) with an optimal cut-off of 17.6%, showing sensitivity and specificity of

**Table 2** Results of logistic regression model evaluating potential predictors of neonatal morbidity and admission to neonatal intensive care unit (NICU) in 939 twin pregnancies that delivered ≥ 34 weeks' gestation

| | *Neonatal morbidity** | | *Admission to NICU* | |
|---|---|---|---|---|
| *Parameter* | *OR (95% CI)* | P | *OR (95% CI)* | P |
| Monochorionic | 1.20 (0.73–1.96) | 0.477 | 1.48 (0.91–2.42) | 0.314 |
| Gestational age at birth (in weeks) | 0.43 (0.37–0.50) | < 0.001 | 0.42 (0.36–0.49) | < 0.001 |
| Birth-weight decile | 0.90 (0.81–0.99) | 0.029 | 0.86 (0.79–0.95) | 0.003 |
| SGA affecting one or both twins | 0.70 (0.38–1.28) | 0.245 | 0.62 (0.35–1.11) | 0.107 |
| Birth-weight discordance (in %) | 1.03 (1.01–1.05) | 0.019 | 1.03 (1.01–1.05) | 0.018 |

*Composite outcome of respiratory morbidity, infectious morbidity, neurological morbidity, hypoglycemia, hypothermia, jaundice, need for phototherapy, necrotizing enterocolitis and retinopathy of prematurity. OR, odds ratio; SGA, small-for-gestational age.

**Table 3** Characteristics of study cohort of 939 twin pregnancies that delivered ≥ 34 weeks' gestation, in those affected *vs* those unaffected by birth-weight (BW) discordance, stratified by degree of discordance

| *Parameter* | *BW discordance ≥ 20% (n = 140)* | *BW discordance < 20% (n = 799)* | P | *BW discordance ≥ 25% (n = 71)* | *BW discordance < 25% (n = 868)* | P |
|---|---|---|---|---|---|---|
| Monochorionic* | 18 (12.9) | 161 (20.2) | 0.094 | 11 (15.5) | 168 (19.4) | 0.530 |
| Gestational age at birth (weeks)† | 36.4 ± 1.3 | 36.7 ± 1.3 | 0.011 | 36.4 ± 1.3 | 36.7 ± 1.3 | 0.062 |
| Birth weight (g)‡ | 2423.8 (2153.8–2673.5) | 2598.0 (2350.0–2840.0) | < 0.001 | 2302.5 (2059.0–2621.3) | 2590.0 (2343.6–2835.0) | < 0.001 |
| Birth-weight decile‡ | 3.35 (1.6–5.7) | 4.70 (2.6–6.6) | < 0.001 | 2.67 (1.5–4.9) | 4.69 (2.6–6.6) | < 0.001 |
| SGA affecting one or both twins* | 116 (82.9) | 305 (38.2) | < 0.001 | 67 (94.4) | 354 (40.8) | < 0.001 |
| Neonatal morbidity*§ | 43 (30.7) | 116 (14.5) | < 0.001 | 28 (39.4) | 131 (15.1) | < 0.001 |
| Admission to NICU* | 50 (35.7) | 137 (17.1) | < 0.001 | 31 (43.7) | 156 (18.0) | < 0.001 |

Data are given as *n* (%), mean ± SD or median (interquartile range). *Compared using chi-square test. †Compared using *t*-test. ‡Compared using Mann–Whitney *U*-test. §Combined outcome of respiratory morbidity, infectious morbidity, neurological morbidity, hypoglycemia, hypothermia, jaundice, need for phototherapy, necrotizing enterocolitis and retinopathy of prematurity. NICU, neonatal intensive care unit; SGA, small-for-gestational age.

**Table 4** Odd ratios (OR) for risk of neonatal morbidity and for admission to neonatal intensive care unit (NICU) in 939 twin pregnancies that delivered ≥ 34 weeks' gestation, at different thresholds of birth-weight (BW) discordance

| | *Neonatal morbidity** | | | | *Admission to NICU* | | | |
|---|---|---|---|---|---|---|---|---|
| *BW discordance threshold* | *Unadjusted OR (95% CI)* | P | *Adjusted OR† (95% CI)* | P | *Unadjusted OR (95% CI)* | P | *Adjusted OR† (95% CI)* | P |
| ≥ 5% | 1.20 (0.82–1.74) | 0.354 | 1.06 (0.68–1.65) | 0.785 | 1.37 (0.96–1.96) | 0.087 | 1.08 (0.71–1.66) | 0.712 |
| ≥ 10% | 1.32 (0.94–1.86) | 0.108 | 1.02 (0.66–1.57) | 0.945 | 1.40 (1.02–1.93) | 0.040 | 1.00 (0.66–1.52) | 0.987 |
| ≥ 15% | 1.94 (1.35–2.78) | < 0.001 | 0.77 (0.48–1.23) | 0.273 | 1.96 (1.39–2.75) | < 0.001 | 0.83 (0.53–1.30) | 0.414 |
| ≥ 20% | 2.61 (1.73–3.93) | < 0.001 | 1.78 (1.05–3.03) | 0.032 | 2.68 (1.81–3.97) | < 0.001 | 1.68 (1.00–2.81) | 0.049 |
| ≥ 25% | 3.66 (2.20–6.11) | < 0.001 | 2.56 (1.33–4.95) | 0.005 | 3.54 (2.15–5.83) | < 0.001 | 2.14 (1.12–4.07) | 0.021 |
| ≥ 30% | 4.97 (2.41–10.29) | < 0.001 | 3.78 (2.12–9.87) | 0.007 | 5.27 (2.55–10.90) | < 0.001 | 5.01 (2.67–9.98) | 0.001 |

*Composite outcome of respiratory morbidity, infectious morbidity, neurological morbidity, hypoglycemia, hypothermia, jaundice, need for phototherapy, necrotizing enterocolitis and retinopathy of prematurity. †Adjusted for chorionicity, birth weight, gestational age at birth and small-for-gestational-age status.

 

35.2% (95% CI, 27.8–43.2%) and 83.2% (95% CI, 80.4–85.8%), respectively (Figure 1 and Table 4). When looking at diagnostic accuracy, intertwin birth-weight discordance of either 20% or 25% showed low sensitivity (27.0% (95% CI, 20.3–34.7%) and 17.6% (95% CI, 12.0–24.4%), respectively) in identifying the twin at risk of neonatal morbidity, while their specificities were 87.6% (95% CI, 85.0–89.8%) and 94.5% (95% CI, 92.7–96.0%), respectively (Table 5).

## DISCUSSION

### Summary of study findings

The findings of this study show that twin pregnancies affected by neonatal morbidity after 34 weeks have greater intertwin birth-weight discordance compared with those not affected. As expected, they were also delivered at an earlier gestational age. The risk of neonatal morbidity increased with increasing degree of birth-weight discordance. Gestational age at birth and birth-weight discordance, but not chorionicity or diagnosis of SGA in either twin, were associated independently

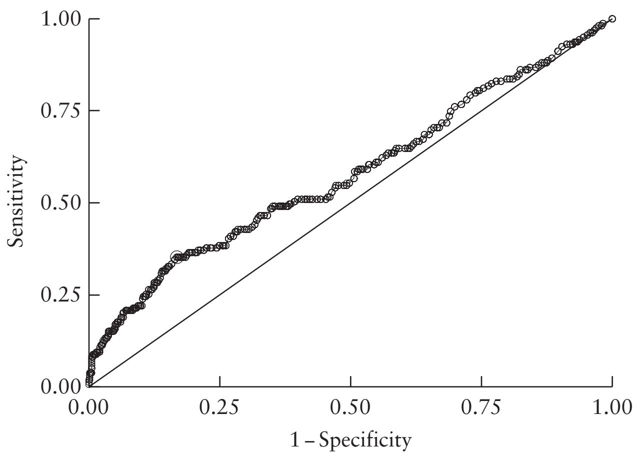


**Figure 1** Receiver–operating characteristics curve for prediction of neonatal morbidity by intertwin birth-weight discordance in 939 twin pregnancies that delivered ≥ 34 weeks' gestation.

with risk of neonatal morbidity. However, when used as a screening tool, intertwin birth-weight discordance ≥ 25% had high specificity but low sensitivity in identifying those twin pregnancies complicated by neonatal morbidity.

### Interpretation of study findings and comparison with existing literature

Despite the fact that the association between intertwin weight discordance and adverse pregnancy outcome is well established, there are no guidelines on how often ultrasound surveillance should be performed in MC and DC twin pregnancies that are affected by growth discordance, and therefore management is usually based on local practice. Several weight-discordance cut-offs have been reported in the published literature to be associated with adverse pregnancy outcome[2–20]. The National Institute for Health and Care excellence (NICE) guidance suggests that fetal weight discordance ≥ 25% should prompt referral to a tertiary fetal medicine center, while the American College of Obstetricians and Gynecologists (ACOG) guidelines use a cut-off of 20% to define significant weight discordance[28,29]. Such differences in the definition of significant weight discordance could be explained by the inclusion of cases affected by anomalies or complications such as TTTS, which are more likely to experience adverse perinatal outcome, differences in the definitions of adverse pregnancy outcome, and lack of stratification of the analysis according to chorionicity and gestational age at assessment and at birth.

We have reported previously that weight discordance was associated independently with the risk of perinatal mortality in twin pregnancies, irrespective of chorionicity[2]. The findings from this study confirm that weight discordance is associated with increased risk of neonatal morbidity, irrespective of chorionicity. This finding may initially seem surprising in view of the reported association between monochorionicity and perinatal morbidity[1]. However, the current analysis included only pregnancies delivering ≥ 34 weeks' gestation, when pregnancy loss or preterm birth due to

**Table 5** Summary estimates of sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, and positive (LR+) and negative (LR−) likelihood ratios of birth-weight (BW) discordance thresholds to predict neonatal morbidity* in 939 twin pregnancies that delivered ≥ 34 weeks' gestation

| *BW discordance threshold* | *Sensitivity (% (95% CI))* | *Specificity (% (95% CI))* | *PPV (% (95% CI))* | *NPV (% (95% CI))* | *LR+ (95% CI)* | *LR− (95% CI)* | *DOR (95% CI)* |
|---|---|---|---|---|---|---|---|
| ≥ 17.6%† | 35.22 (27.8–43.2) | 83.21 (80.4–85.8) | 29.95 (23.5–37.1) | 86.30 (83.6–88.7) | 2.10 (1.6–2.7) | 0.78 (0.68–0.87) | 2.69 (1.8–4.0) |
| ≥ 5% | 71.70 (64.0–78.6) | 32.05 (28.8–35.5) | 17.70 (14.8–20.9) | 84.75 (80.1–88.7) | 1.06 (0.93–1.16) | 0.88 (0.67–1.14) | 1.19 (0.8–1.7) |
| ≥ 10% | 50.94 (42.9–59.0) | 56.03 (52.5–59.5) | 19.10 (15.5–23.2) | 84.85 (81.5–87.8) | 1.16 (0.97–1.36) | 0.88 (0.73–1.02) | 1.32 (0.9–1.9) |
| ≥ 15% | 37.74 (30.2–45.8) | 76.15 (73.0–79.1) | 24.39 (19.2–30.3) | 85.71 (82.9–88.2) | 1.58 (1.20–1.99) | 0.82 (0.71–0.92) | 1.94 (1.3–2.8) |
| ≥ 20% | 27.04 (20.3–34.7) | 87.56 (85.0–89.8) | 30.71 (23.2–39.1) | 85.48 (82.9–87.9) | 2.17 (1.57–2.96) | 0.83 (0.75–0.91) | 2.61 (1.7–4.0) |
| ≥ 25% | 17.61 (12.0–24.4) | 94.49 (92.7–96.0) | 39.44 (28.0–51.8) | 84.91 (82.4–87.2) | 3.19 (2.04–4.94) | 0.87 (0.80–0.93) | 3.66 (2.1–6.3) |
| ≥ 30% | 9.43 (5.4–15.1) | 97.95 (96.7–98.8) | 48.39 (30.2–66.9) | 84.14 (81.6–86.5) | 4.60 (2.34–8.96) | 0.92 (0.87–0.96) | 4.97 (2.2–11.0) |

*Composite outcome of respiratory morbidity, infectious morbidity, neurological morbidity, hypoglycemia, hypothermia, jaundice, need for phototherapy, necrotizing enterocolitis, retinopathy of prematurity. †Optimal cut-off based on receiver–operating characteristics curve. DOR, diagnostic odds ratio.

 

complications associated with monochorionicity, such as TTTS, is unlikely to occur. Regardless, the management of growth-discordant twins should take into account chorionicity in view of the higher risk of mortality and adverse neurological outcome observed in cases of cotwin demise in MC pregnancies[30].

## Clinical and research implications

Intertwin weight discordance is among the major determinants of perinatal outcome in twin pregnancy. If assessment of chorionicity during the first trimester of pregnancy is fundamental to stratifying the obstetric risk and tailoring the antenatal management of these pregnancies, assessment of the degree of weight discordance during the third trimester is warranted to anticipate the risk of fetal loss and adverse pregnancy outcome, and to ensure that an appropriate follow-up and delivery plan are in place.

Furthermore, the degree of weight discordance associated with adverse pregnancy outcome has been shown to be related to gestational age at ultrasound, thus suggesting the need for gestational age-specific cut-offs or the use of reference ranges of weight discrepancy according to gestational age at assessment.

Finally, although associated independently with pregnancy outcome, weight discordance *per se* should not be used as a primary indication for delivery, as shown by its poor predictive accuracy for perinatal mortality and morbidity[31,32]. In this scenario, early iatrogenic delivery will reduce the risk of mortality but will increase the risk of morbidity, since gestational age at birth remains the main determinant of perinatal outcome in twin pregnancies[2].

The pathophysiology of discordant growth is different in MC and DC twin pregnancies. While the fact that discordant growth in DC twin pregnancies is caused mainly by discordant placental size and function, in MC twin pregnancy, the magnitude of discordant growth is influenced not only by abnormal placental sharing, but also by the direction of blood flow interchange through the placental anastomoses[33]. Therefore, prenatal detection of discordant growth in a MC twin pregnancy should prompt careful Doppler evaluation of the umbilical artery flow pattern in order to stratify the risk of adverse pregnancy outcome[34]. Conversely, the management of weight discordance in a DC twin pregnancy should be tailored primarily according to gestational age. In this scenario, early iatrogenic delivery is likely to increase the risk of perinatal morbidity, given the overall small risk of mortality in twins affected by discordant growth.

In the present study, weight discordance was associated independently with perinatal morbidity, while SGA, defined using twin-specific growth charts, was not. This finding has been also reported by other studies on weight discordance in twin pregnancies and may seem initially surprising because low birth weight is recognized universally as an independent contributor to perinatal mortality and morbidity in singletons[35]. The pathophysiology of this association has not yet been clearly elucidated, but it is plausible that weight discordance may represent a status of abnormal placental development and sharing between the two twins, leading to an aberrant growth pattern and increased risk of adverse perinatal outcome, irrespective of weight centile. Further studies exploring the growth trend in twins affected by weight discordance are needed in order to provide a pathophysiological rationale for this finding.

## Strengths and limitations

The strengths of this study include, firstly, the large sample size, secondly, exclusion of cases affected by an anomaly or TTTS, thirdly, assessment of the strength of the association of weight discordance with and its predictive accuracy for neonatal morbidity and, fourthly, stratification of the analysis including only twins born after 34 weeks of gestation in order to reduce the contribution of gestational age at birth to determining perinatal outcome. The retrospective design of the study and assessment of a composite score for neonatal morbidity in order to acquire statistical power represent its main limitations. Furthermore, although the inclusion of twins born only $\geq$ 34 weeks theoretically reduced the actual independent contribution of gestational age to the observed outcomes, gestational age at birth remained associated independently with risk of neonatal morbidity. Therefore, the differences observed in the study groups might have been the result of late preterm birth rather than weight discordance *per se*. Another limitation of the study was the lack of stratification according to the severity of the different explored outcomes in view of the small number of events per outcome, which would have lowered the power of the analysis. Unfortunately, we could not stratify the analysis according to different gestational ages at birth as it would have reduced the power of the analysis, which might have led to misleading results. Finally, fetal Doppler data were not available for all cases in the current analysis. However, twin pregnancies complicated by marked selective fetal growth restriction and abnormal Doppler findings are generally delivered before 34 weeks of gestation. Therefore, it is unlikely that our study cohort would have contained twin pregnancies with abnormal umbilical artery Doppler findings.

## Conclusions

Weight discordance is associated independently with the risk of neonatal morbidity in twins born from 34 weeks' gestation, irrespective of chorionicity. However, its predictive accuracy for neonatal morbidity is poor. Large prospective multicenter studies sharing the same protocol for antenatal management are needed to ascertain the actual contribution of intertwin weight discordance to the risk of neonatal morbidity and to determine whether different weight discordance thresholds should be used at different gestational ages.

 

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## SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

**Table S1** Incidence of individual components of neonatal morbidity in 939 twin pregnancies that delivered $\geq$ 34 weeks' gestation

 