Definition of Intertwin Birth Weight Discordance

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OBJECTIVE: To establish the level of birth weight discordance at which perinatal morbidity increases in monochorionic and dichorionic twin pregnancy.

METHODS: This prospective multicenter cohort study included 1,028 unselected twin pairs recruited over a 2-year period. Participants underwent two weekly ultrasonographic surveillance from 24 weeks of gestation with surveillance of monochorionic twins two-weekly from 16 weeks. Analysis using Cox proportional hazards compared a composite measure of perinatal morbidity (including any of the following: mortality, respiratory distress syndrome, hypoxic–ischemic encephalopathy, periventricular leukomalacia, necrotizing enterocolitis, or sepsis) at different degrees of birth weight discordance with adjustment for chorionicity, gestational age, twin–twin transfusion syndrome, birth order, gender, and growth restriction.

RESULTS: Perinatal outcome data were recorded for 977 patients (100%) who continued the study with both fetuses alive beyond 24 weeks, including 14 cases of twin–twin transfusion syndrome. Adjusting for gestation at delivery, twin order, gender, and growth restriction, perinatal mortality, individual morbidity, and composite perinatal morbidity were all seen to increase with birth weight discordance exceeding 18% for dichorionic pairs (hazard ratio 2.2, 95% confidence interval [CI] 1.6–2.9, $P<.001$) and 18% for monochorionic twins without twin–twin transfusion syndrome (hazard ratio 2.6, 95% CI 1.6–4.3, $P<.001$). A minimum twofold increase in risk of perinatal morbidity persisted even when both twin birth weights were appropriate for gestational age.

CONCLUSION: The threshold for birth weight discordance established by this prospective study is 18% both for dichorionic twin pairs and for monochorionic twins without twin–twin transfusion syndrome. This threshold is considerably lower than that defined by many retrospective series as pathologic. We suggest that an anticipated difference of 18% in birth weight should prompt more intensive fetal monitoring.

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LEVEL OF EVIDENCE: II

Twin gestations are consistently overrepresented in all facets of perinatal morbidity and mortality in the developed world. Some studies have identified discordant twin growth as an independent risk factor for adverse perinatal outcome,[1–4] whereas others have attributed the morbidity and mortality observed in size-discordant pairs to confounding factors such as gestational age at delivery, actual birth weight, and

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gender discordance.[5–7] The inclusion of cases of twin–twin transfusion syndrome and selective fetal growth restriction in many twin cohorts renders it difficult to ascertain whether twin growth discordance is a distinct entity that independently confers risk of adverse perinatal outcome or simply a consequence of differing twin growth patterns that may or may not be pathologic.

Prenatal recognition of twin growth discordance can lead to iatrogenic preterm delivery, thus conferring the sequelae of prematurity not only on the growth-restricted twin, but also on the normally grown cotwin, yet there is a lack of agreement on a threshold disparity in fetal weights that constitutes "discordant growth." Suggested thresholds for significant intratwin birth weight discordance, all established from retrospective series (Table 1), range from 10% to 30%.[2,8–15]

The objective of this prospective study was to establish a threshold for birth weight discordance in monochorionic and in dichorionic twin pregnancies.

MATERIALS AND METHODS

The prospective Evaluation of Sonographic Predictors of Restricted growth In Twins study was conducted at eight academic perinatal centers in Ireland, all with tertiary neonatal intensive care facilities, from May 2007 to October 2009. Institutional review board approval was obtained at each participating site and the study participants gave written informed consent. Inclusion criteria for this study were all diamniotic twin pregnancies enrolled before 22 weeks of gestation with both fetuses alive with intact membranes at 24 weeks and without major fetal structural abnormality (either suspected or confirmed).

All patients meeting inclusion criteria were subjected to a program of intensive fetal surveillance carried out by dedicated research ultrasonographers using standardized ultrasonographic equipment (GE Voluson Expert 730). Ultrasonographic examination included biometry, placental location and number, Doppler parameters, and cord insertion site.

Chorionicity was assigned by standard ultrasonographic criteria (placental number, identification of lambda or T sign, intertwin membrane thickness, and determination of fetal gender) at the first ultrasonographic evaluation and subsequent correlation was sought with placental pathologic examination. Two-weekly growth scans were performed from 16 weeks of gestation until delivery for monochorionic twin pairs and from 24 weeks until delivery in dichorionic pregnancies. Umbilical arterial and middle cerebral arterial Doppler waveforms were recorded in addition to standard biometry (abdominal circumference, biparietal diameter, head circumference, femur length) and documentation of the deepest vertical pocket of amniotic fluid in each sac. An arbitrary definition of discordance of 20% was selected to inform the extent of Doppler monitoring insofar as analysis of the ductus venosus waveform was included in the 2-weekly ultrasonographic surveillance in the event that 20% discordance was identified. The ductus venosus waveform was also recorded in the event of absence or reversal of end-diastolic flow in the umbilical artery or evidence of cephalization of cerebral blood flow or "brain-sparing" (middle cerebral artery resistance index to umbilical artery resistance index less than 1.0). A quality review system was in place, requiring regular submission by ultrasonographers of images and Doppler traces to a central ultrasonography quality assurance committee.

At each ultrasonography examination, the presence or absence of obstetric complications or clinical events was recorded (hypertension, preeclampsia,

Table 1. Meta-Analysis of Studies Investigating Clinical Significance of Twin Intrapair Birth Weight Differences

Author	Year	Study Design	Analysis by Chorionicity	Definition of Discordance
Amaru et al[13]	2004	Retrospective cohort	Yes	20%
Hartley et al[2]	2002	Population-based retrospective analysis	No	25%
Demissie et al[10]	2002	Retrospective cohort	No	10% for smaller twin 20% for larger twin
Redman et al[14]	2002	Retrospective cohort	No	30%
Victoria et al[11]	2001	Retrospective cohort	Yes	Greater than 25% ("severe discordance") 5–25% ("mild discordance")
Hollier et al[15]	1999	Retrospective cohort	No	25%
Lanni et al[12]	1998	Retrospective cohort	No	24% (90th centile) 29% (95th centile)
Erkkola et al[9]	1985	Retrospective cohort	No	25%

rupture of membranes, gestational diabetes, antepartum hemorrhage, threatened preterm labor, hospital admission, and the administration of antenatal corticosteroids for fetal lung maturity). All prenatal and ultrasonographic data were contemporaneously transferred to an ultrasonography software system (Viewpoint) and uploaded onto a live web-based central consolidated database. Management decisions, including those relating to timing and mode of delivery, were at the discretion of the lead clinician managing each twin case.

Pediatric outcomes for all twins not requiring neonatal intensive care were recorded by research staff at 28 days of life and uploaded onto the consolidated database. Newborns requiring neonatal intensive care admission had their outcomes recorded by neonatology medical or nursing staff on discharge from the hospital.

Perinatal mortality was defined as death of a neonate weighing at least 500 g or who attained a gestational age of at least 24 completed weeks occurring either in utero or within the first 28 days of life. Gestational age at the time of in utero death was determined by ultrasonography.

Neonatal intensive care unit or special care baby unit admission was used as an indicator for neonatal morbidity and length of neonatal ward stay was recorded. In addition, a composite measure of adverse perinatal outcome included any of the following: mortality, hypoxic–ischemic encephalopathy, periventricular leukomalacia, necrotizing enterocolitis, respiratory distress, or sepsis. A diagnosis of hypoxic–ischemic encephalopathy was recorded in the setting of profound umbilical arterial acidemia (pH <7), persistence of an Apgar score of 3 or less for longer than 5 minutes, neonatal neurologic sequelae, and multiple organ involvement. Periventricular leukomalacia was diagnosed by neonatal ultrasonography and confirmed by subsequent magnetic resonance imaging. A diagnosis of respiratory distress was considered for any neonate requiring invasive or noninvasive respiratory support, was supported by radiographic criteria where available, and length of oxygen-dependence recorded. A diagnosis of neonatal sepsis was made when appropriate clinical features were confirmed by positive microbiologic cultures.

All placentae underwent detailed pathologic examination according to a standardized protocol that included final determination of chorionicity.

Birth weight discordance was calculated by using the formula (larger twin weight−smaller twin weight)/larger twin weight$\times$100. Twins were classified as small for gestational age if one or both neonates were less than the fifth centile at birth by singleton Doubilet norms[16] and appropriate for gestational age if neither twin weighed less than the fifth centile at birth. Doubilet norms[16] represent a birth weight table generated from a cohort of neonates who had accurate gestational age assignment by first-trimester ultrasonography.

Using the statistical methods outlined subsequently, a threshold for significant birth weight discordance associated with increased risk of adverse perinatal outcome was determined. This analysis was conducted separately for monochorionic and for dichorionic twins. In the case of the monochorionic cohort, this threshold was re-examined with exclusion of cases of twin–twin transfusion syndrome.

The significance of birth weight discordance was further determined separately for those pregnancies in which both twins were appropriately grown for gestational age (both twin birth weights greater than the fifth centile and less than the 95th centile by Doubilet norms) and for those cases in which one twin of a pair was deemed small for gestational age (ie, fifth centile or less). The gestational age of the twin pair, birth order, and gender were used as adjusting variables in the regression models when estimating the risk of perinatal mortality or morbidity associated with birth weight discordance.

Statistical comparisons between groups were made using the chi-square test for nominal variables and the Wilcoxon rank-sum test for ordinal and continuous variables. Based on the sample size in our cohort, the study was sufficiently powered (80% power for monochorionic twins, 99% power for dichorionic twins) to detect a risk ratio of 2 in either monochorionics or dichorionics. This is based on the assumption of a minimum adverse outcome prevalence (in a comparative control group) of 4% and 14% in dichorionics and monochorionics, respectively. Adverse perinatal outcomes with lower prevalence rates require greater risk ratios to be detectable.

Cox proportional hazards models were used to analyze morbidity outcomes and the predictive ability of birth weight discordance stratified according to study center. The Cox models analyzed twin outcomes individually (ie, n=2 for each twin pair) and a robust sandwich estimator for variance[17] was used to account for the natural pairing in the data. Each discordance cutoff (up to 30% birth weight discordance) was analyzed separately and statistical significance of birth weight discordance was set at the nominal 1% level. *P* values were then adjusted using the Bonferroni method for multiple comparisons. The statistical software SAS 9.1 was used for analysis.

RESULTS

A total of 1,001 twin pregnancies recruited during the 2-year study period (May 2007 to October 2009) completed the prenatal fetal surveillance schedule and delivered at one of the eight participating perinatal centers. An additional 27 recruited patients did not complete the study as a result of transfer of obstetric care to a nonparticipating center, withdrawal from the study, or research staff shortage leading to inability to complete the ultrasonographic surveillance protocol. Previability single or dual fetal death was identified in 24 pairs such that perinatal outcome data were recorded on 100% (977 of 977) of participants who had two live fetuses with intact membranes at 24 weeks of gestation without suspicion for major structural or chromosomal abnormality. Within this cohort, 14 pregnancies were complicated by twin–twin transfusion syndrome.

Chorionicity was reassigned according to placental pathology examination in 17 of 977 cases (1.7%) such that the proportion of twins that was designated as monochorionic and dichorionic was 19% (188 of 977) and 81% (789 of 977), respectively.

Median gestational age at recruitment was 16 weeks (interquartile range, 13–19 weeks). Mean birth weight discordance was 13.2% (range, 0.1–53%) and 11.4% (range, 0–58%) for monochorionic and dichorionic twin pairs, respectively. Birth weights were both above the fifth centile and below the 95th centile for gestational age and thus deemed appropriate for gestational age in 819 of 977 cases (84%). One twin of a pair weighed less than the fifth centile and was thus small for gestational age in 108 of 977 pregnancies (11%). Birth weight at or above the 95th centile for gestational age in one twin of a pair was identified among 25 of 977 (2.5%) pairs. Both birth weights within a twin pair were deemed small for gestational age or large for gestational age, respectively, in 10 of 977 (1%) and one of 977 (0.1%) cases.

Maternal and obstetric characteristics of the study cohort with respect to varying degrees of birth weight discordance are depicted in Table 2. Greater degrees of intertwin birth weight discordance were associated with older maternal age, nulliparity, assisted conception, pregnancy-induced hypertension, and noncentral placental cord insertion site for either twin.

Table 2. Maternal and Obstetric Characteristics of the Study Population According to Intertwin Birth Weight Discordance (N=977)

Characteristic	All (N=977)	15% or Greater Discordance (n=301)	20% or Greater Discordance (n=168)	25% or Greater Discordance (n=91)	30% or Greater Discordance (n=55)
Maternal age (y)	33	33	34	34*	35†
Parity (one or more births)	495 (52)	145 (50)	80 (49)	40 (44)	18 (33)‡
Nonwhite ethnicity	61 (7)	14 (5)	8 (6)	6 (8)	4 (10)
Assisted conception	233 (27)	76 (29)	47 (32)	30 (37)*	19 (41)*
Monochorionic	187 (19)	68 (23)	38 (23)	22 (24)	15 (27)
Previous cesarean delivery	88 (9)	29 (10)	18 (11)	9 (10)	5 (9)
Smoking	112 (12)	34 (12)	20 (13)	11 (13)	4 (8)
Body mass index (kg/m^2)	24.4	24.6	24.7	24.5	25.3
Spontaneous labor	296 (30)	75 (25)*	37 (22)*	18 (20)*	8 (15)†
Preterm premature rupture of fetal membranes	24 (2)	7 (2)	6 (4)	3 (3)	2 (4)
Hypertension or PET	130 (13)	53 (18)†	30 (18)	13 (14)	8 (15)
Pregestational diabetes	7 (<1)	4 (1)	1 (<1)	1 (1)	0
Gestational diabetes	17 (2)	6 (2)	4 (2)	2 (2)	1 (2)
First-trimester bleeding	110 (11)	31 (10)	17 (11)	9 (10)	5 (9)
Antepartum hemorrhage, placental abruption, placenta praevia	66 (7)	23 (8)	12 (7)	5 (5)	4 (7)
Gestational age at delivery	37 0/7	36 2/7‡	35 6/7‡	35 0/7‡	34 5/7‡
Noncentral cord insertion	238 (32)	76 (35)	49 (41)*	24 (39)	13 (35)

PET, preeclamptic toxemia.
Data are median or n (%).
Study population (n=977) includes all pregnancies with both fetuses alive beyond 24 weeks of gestation. Unavailable data for parity (n=17), ethnicity (n=120), assisted conception (n=122), smoking status (n=44), and cord insertion site (n=215).
Statistical significance using the Wilcoxon rank-sum test or χ^2 test where appropriate.
* 5% level ($P<.05$).
† 1% level ($P<.01$).
‡ 0.1% level ($P<.001$).
Comparisons are between the discordant group and those with lesser degrees of discordance.

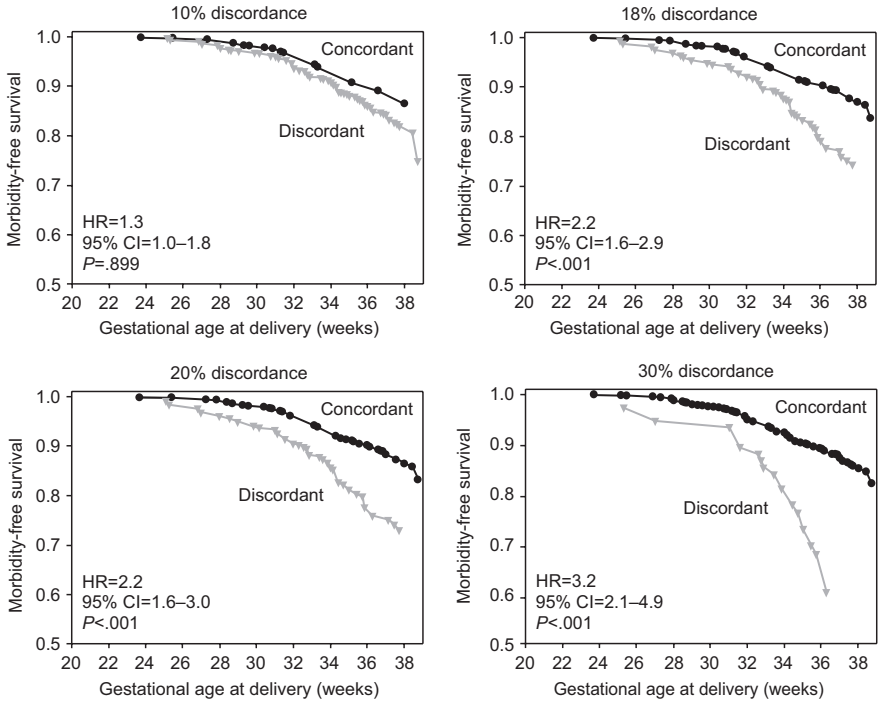

Fig. 1. Kaplan-Meier morbidity-free survival curves and birth weight discordance for dichorionic twins (n=1,578). "Concordant" refers to those twins with less than each sample level of discordance. Composite measure of adverse perinatal outcome includes any of the following: mortality, hypoxic–ischemic encephalopathy, periventricular leukomalacia, necrotizing enterocolitis, respiratory distress, or sepsis. HR, hazard ratio; CI, confidence interval.

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Adjusting for gestational age at delivery, perinatal mortality, individual perinatal morbidity, and composite perinatal morbidity were all seen to increase in association with intertwin birth weight discordance in excess of 15% for monochorionic pairs (hazard ratio 2.9, 95% confidence interval [95% CI] 2.0–4.4, *P*<.001) and 18% for dichorionic pairs (hazard ratio 2.2, 95% CI 1.6–2.9, *P*<.001). Twin–twin transfusion syndrome accounted for the disparity between these cutoff levels of discordance, because exclusion of all 14 twin cases with prenatal stigmata of twin–twin transfusion syndrome resulted in a threshold of 18% for significant intertwin birth weight discordance for both dichorionic twins and for monochorionic twins without twin–twin transfusion syndrome (Figs. 1 and 2).

Absolute morbidity risks were higher among discordant monochorionic twins when compared with discordant dichorionic twins at every level of birth weight discordance as illustrated by the larger spatial differences between the Kaplan-Meier curves for monochorionic twins in Figure 3.

Individual and composite perinatal morbidity in relation to these established threshold discordance levels are outlined in Table 3 for dichorionic twins and in Table 4 for monochorionic twins without twin–twin transfusion syndrome.

For the cohort excluding twin–twin transfusion syndrome cases (N=963 pairs), the 18% cutoff for significant birth weight discordance corresponded to a statistically significant doubling in the risk of adverse perinatal outcome (hazard ratio 2.3, 95% CI 1.8–2.9, *P*<.001). At this 18% discordance level, the subgroup deemed appropriate for gestational age (N=819) also had a doubling in the risk of perinatal morbidity (hazard ratio 2.1, 95% CI 1.6–2.8, *P*<.001). However, at the 18% level of discordance, the group in which one twin of a pair was deemed small for gestational age (less than the fifth percentile, n=108) had more than four times the risk of perinatal morbidity (hazard ratio 4.5, 95% CI 1.8–10.8), although the statistical significance was not strong as a result of the small sample size (*P*=.024).

Table 5 demonstrates the risk of adverse perinatal outcome associated with a twin fetus being small for gestational age 5th percentile or less and those associated with intertwin birth weight discordance of at least 18%. Interestingly, small for gestational age 5th percentile or less in the dichorionic group is not predictive at all (hazard ratio 1.0, 95% CI 0.7–1.6, *P*<.928). On the other hand, 18% birth weight discordance confers a doubling of the risk of adverse outcomes (hazard ratio 2.2, 95% CI 1.6–2.9, *P*<.001) for dichorionic twins. Small for gestational age carries a risk of adverse perinatal outcome in the monochorionic group (hazard ratio 2.6, 95% CI 1.4–4.7, *P*<.003) that is comparable to the risk associated with 18% discordance (hazard ratio 2.6, 95% CI 1.6–4.3, *P*<.001). As illustrated, the greatest perinatal risk

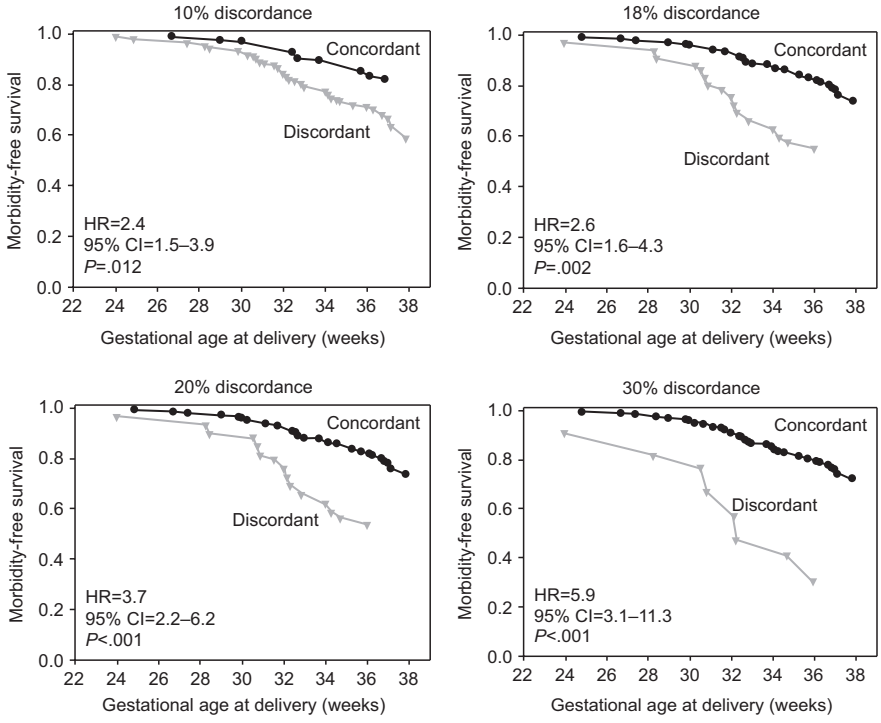

Fig. 2. Kaplan-Meier morbidity-free survival curves and birth weight discordance for monochorionic twins without twin–twin transfusion syndrome (n=320). "Concordant" refers to those twins with less than each sample level of discordance. Composite measure of adverse perinatal outcome includes any of the following: mortality, hypoxic–ischemic encephalopathy, periventricular leukomalacia, necrotizing enterocolitis, respiratory distress, or sepsis. HR, hazard ratio; CI, confidence interval.

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seems to occur among twins where one twin is small for gestational age (less than the fifth percentile) and its cotwin is at least 18% larger.

This comparative analysis demonstrates that small for gestational age at the 5% level confers a much lower estimated risk of adverse perinatal outcome than 18% birth weight discordance among dichorionic twins, whereas small for gestational age (5th percentile or less) and 18% discordance confer comparable risks among monochorionic twins without twin–twin transfusion syndrome.

Among all twins, neither gender (P=.61) nor birth order (P=.27) demonstrated a difference in the prediction of morbidity, whereas adverse perinatal outcome was as likely to affect the larger twin as the smaller twin of a discordant pair (P=.29).

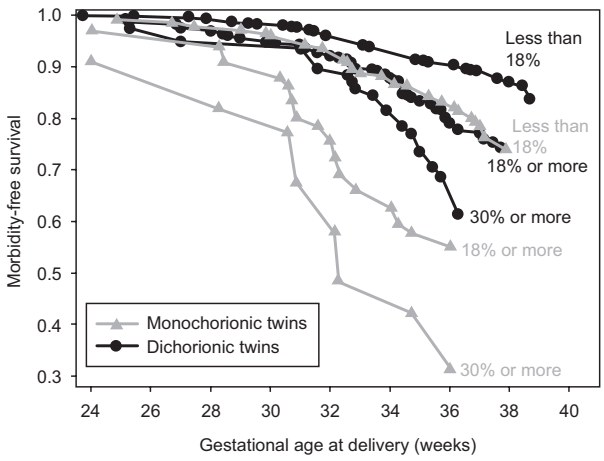

Fig. 3. Morbidity-free survival and birth weight discordance in monochorionic twins without twin–twin transfusion syndrome and dichorionic twins.

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DISCUSSION

This large multicenter prospective study found that the threshold for growth discordance is 18% both for dichorionic twin pairs and for monochorionic twins without twin–twin transfusion syndrome. The existing evidence for a relationship between intertwin birth weight discordance and adverse perinatal outcome is conflicting, not least in its definition of discordant growth. This study, aimed at identifying a clinically relevant threshold for discordant growth, is among the largest prospective cohort studies of twins published to date with complete perinatal outcome ascertainment on all study participants.

The mechanism whereby two fetuses exposed to the same intrauterine environment should adopt different growth patterns, resulting in "growth discordance," represents a final common pathway for several twin pregnancy phenomena. In the case of

Table 3. Dichorionic Twins: Perinatal Mortality and Morbidity by Birth Weight Discordance (18% Threshold) Adjusted for Gestational Age at Delivery (N=1,578)

	Concordant (Less Than 18% BW Discordance) (n=1,244)	Discordant (18% or Greater BW Discordance) (n=334)			*P*		
		Smaller Twin (n=167)	Either Twin (n=334)	Larger Twin (n=167)	Smaller Twin	Either Twin	Larger Twin
Gestational age at delivery (wk)	37.1 (35.9–38.0)	36.3 (34.4–37.7)				<.001	
Mortality	0	3 (1.8)	5 (1.5)	2 (1.2)	<.002	<.001	<.014
NICU admission	458 (37)	102 (61)	187 (56)	85 (51)	<.001	<.001	.004
HIE	0	0	1 (0.3)	1 (0.6)	—	<.212	<.119
IVH	12 (1.0)	2 (1.2)	7 (2.1)	5 (3.0)	<.678	<.152	.024
PVL	2 (0.2)	0	1 (0.3)	1 (0.6)	1.000	<.511	<.315
NEC	2 (0.2)	2 (1.2)	5 (1.5)	3 (1.4)	<.072	.006	<.014
RDS	133 (11)	24 (14)	61 (18)	37 (22)	<.156	<.001	<.001
Sepsis	47 (3.8)	14 (8)	27 (8.1)	13 (7.8)	<.006	<.001	.016
Composite adverse perinatal outcome (mortality, HIE, IVH, PVL, NEC, RDS, sepsis)	143 (12)	31 (19)	72 (22)	41 (25)	<.001	<.001	<0.001

BW, body weight; NICU, neonatal intensive care unit; HIE, hypoxic–ischemic encephalopathy; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia; NEC, necrotizing enterocolitis; RDS, respiratory distress syndrome.
Data are median (interquartile range) or n (%) unless otherwise specified.

monochorionic twin pregnancy, postulated mechanisms for discordant growth include twin–twin transfusion syndrome or unequal placental sharing. The latter phenomenon is thought to result from unequal splitting of the initial cell mass.[18] Dichorionic twins may be complicated by placental pathology localized to one placenta only.

Owing to potential inherent differences in twin genotype or placental function, it must be acknowledged that some degree of birth weight discordance should be anticipated. Published retrospective series indicate that a 10% difference in fetal weight between cotwins should be considered to represent the norm.[5,19] However, what constitutes discordant growth?

Table 4. Monochorionic Twins: Perinatal Mortality and Morbidity by Birth Weight Discordance (18% Threshold) Adjusted for Gestational Age at Delivery Excluding Twin–Twin Transfusion Syndrome (n=348)

	Concordant (Less Than 18% BW Discordance) (n=266)	Discordant (18% or Greater BW Discordance) (n=82)			*P*		
		Smaller Twin (n=41)	Either Twin (n=82)	Larger Twin (n=41)	Smaller Twin	Either Twin	Larger Twin
Gestational age at delivery (median and IQR)	36.1 (34.7–37.1)	34.7 (32.1–36.7)				<.028	
Mortality	4 (1.5)	2 (4.9)	3 (3.7)	1 (2.4)	<.185	<.363	<.515
NICU admission	134 (50)	29 (71)	55 (67)	26 (63)	<.016	.008	<.111
HIE	1 (0.4)	0	0	0	1.000	1.000	1.000
IVH	7 (2.6)	1 (2.4)	3 (3.7)	2 (4.9)	1.000	<.706	<.344
PVL	0	0	0	0	—	—	—
NEC	2 (0.8)	1 (2.4)	1 (1.2)	0	<.351	<.555	1.000
RDS	40 (15)	13 (32)	25 (30)	12 (29)	<.009	<.002	<.024
Sepsis	25 (9)	5 (12)	9 (11)	4 (10)	<.573	<.675	1.000
Composite adverse perinatal outcome (mortality, HIE, IVH, PVL, NEC, RDS, sepsis)	53 (20)	16 (39)	29 (35)	13 (32)	<.007	.004	<.088

BW, body weight; IQR, interquartile range; NICU, neonatal intensive care unit; HIE, hypoxic–ischemic encephalopathy; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia; NEC, necrotizing enterocolitis; RDS, respiratory distress syndrome.
Data are median (interquartile range) or n (%) unless otherwise specified.

Table 5. Comparative Analysis of Small for Gestational Age Less Than the Fifth Centile and Intertwin Birth Weight Discordance 18% or Greater

	SGA 5%		18% BW Discordance		18% BW Discordance Excluding SGA	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Monochorionics (excluding twin–twin transfusion syndrome)	2.6 (1.4–4.7)	<.003	2.6 (1.6–4.3)	<.001	2.2 (1.3–4.0)	<.006
Dichorionics	1.0 (0.7–1.6)	.928	2.2 (1.6–2.9)	<.001	2.1 (1.5–2.9)	<.001

SGA, small for gestational age; BW, birth weight; HR, hazard ratio; CI, confidence interval.

Studies that have sought to identify a cutoff for discordant growth have all been retrospective and the variation in reported "significant" thresholds for discordant growth may be explained by a number of factors. Inclusion of cases of major congenital fetal abnormality or fetal aneuploidy will inevitably affect any perceived discordance-related morbidity given the strong association between fetal structural abnormalities and aberrant growth patterns. Furthermore, many series do not acknowledge the critical contribution that chorionicity makes to twin growth and to twin-related morbidity. Growth discordance is one of the key defining features of twin–twin transfusion syndrome, a condition that confers a high risk of twin mortality and severe perinatal morbidity. This concern underpins our rationale for establishing a threshold for significant birth weight discordance separately for monochorionic and for dichorionic twins and, furthermore, for monochorionic twins without twin–twin transfusion syndrome.

Our study demonstrates that a threshold level of 18% discordance between cotwin birth weights represents the cutoff above which there exists at least a doubling in risk of adverse perinatal outcome. It is important to emphasize that although the 18% threshold applies both to dichorionic pregnancies and to monochorionic twins without twin–twin transfusion syndrome, the absolute risks are higher for monochorionic twins when compared with dichorionic twins at every level of birth weight discordance. Indeed, dichorionic twins with greater than 18% discordance have a similar risk profile to concordant monochorionic twins.

Several studies indicate that the principal determinants of outcome are actual birth weight and gestational age at delivery[5,6,20,21] rather than intrapair size difference per se. We therefore adjusted all analyses for gestational age at delivery and established the threshold for significant birth weight discordance (18%) within the subcohort of 819 twin pairs that were appropriately grown for gestational age. Within the smaller subcohort of twin pairs that contained a growth restricted cotwin below the fifth percentile, the 18% threshold conferred a fourfold increased risk of adverse perinatal outcome when compared with concordant twins. Therefore, although morbidity risks may be highest in the setting of a twin pair that is discordant for fetal growth restriction, the risk of adverse perinatal outcome remains increased within a growth-discordant pair even where both twins measure within range.

In clinical practice, management decisions relating to level of fetal surveillance, antenatal corticosteroid therapy, and indeed timing of delivery are frequently driven by the smaller twin of a discordant pair, yet it is interesting to note that the adverse perinatal outcome described in this study was equally shared by the smaller and the larger twin of a discordant pair. Twin–twin transfusion syndrome did not account for increased risk for the larger twin, because this observation held true when twin–twin transfusion syndrome cases were excluded. Our finding that among discordant pairs, either twin may experience adverse perinatal outcome is consistent with that published by Hartley et al[2] in a large population-based retrospective analysis of linked birth certificates and neonatal death certificates. Several studies have demonstrated an increased risk for short-term transient respiratory morbidity among heavier twins compared with gestation-matched lighter twins.[22,23] Recognition that the larger twin may be at equal risk to the smaller twin of a discordant pair is important in the prenatal counseling of parents, who commonly perceive that the smaller twin is more susceptible to perinatal morbidity.

The strengths of this study lie in its prospective nature with resultant elimination of selection bias and complete data ascertainment together with a short study period (2 years) that allows for accurate reflection of contemporary perinatal practice. The inherent differences in etiology of discordant growth in monochorionic and in dichorionic twin gestations are acknowledged through accurate determination of

chorionicity with ultrasonography and placental examination.

A limitation of our study is the small number of serious adverse perinatal outcomes within this intensively monitored cohort. Furthermore, it is unclear to what extent, if any, the ultrasonographic surveillance strategy adopted for this study may have minimized the number of adverse perinatal events. However, it is unlikely that the cutoff for significant birth weight discordance established by this study represents an underestimate, because the threshold established is notably lower than that reported in the vast majority of retrospective series to date.[2,9–14] Our study did not find that the nonpresenting twin carried a higher risk for perinatal morbidity than its presenting cotwin, in contrast to published UK population-based birth outcome data,[24] although this may be a consequence of insufficient numbers.

Given the independent contribution that intrapair size discordance makes to adverse perinatal outcome, a strategy of heightened fetal surveillance is justified in pregnancies with prenatally identified intertwin growth discordance. However, clinical management of growth-discordant twin pregnancies relies on accurate prenatal recognition of at-risk twin pairs. Studies of serial biometry for the detection of discordant growth have yielded conflicting reports of accuracy,[19,25] and the optimal interval for such examinations, or the parameters most predictive of discordance are not clear. Any proposed intervention aimed at reducing discordance-related perinatal morbidity must address the refinement of prenatal prediction as a priority. Importantly, the definition of discordant twin growth represents the first step in addressing the prenatal management of pregnancies complicated by this phenomenon and analysis of the most worthy individual or composite ultrasonographic parameters for prenatal prediction of discordance is beyond the scope of this article.

In conclusion, despite their shared intrauterine milieu, twin growth is frequently mismatched. Irrespective of the proven or postulated etiology for twin growth discordance, there exists a threshold discordance level, 18% as defined by this study, which should be considered abnormal in all types of twins. Where this level of discordance is recognized in the prenatal period, heightened fetal surveillance should be instituted.

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