Optimum Timing for Planned Delivery of Uncomplicated Monochorionic and Dichorionic Twin Pregnancies

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OBJECTIVE: To determine the optimum timing for planned delivery of uncomplicated monochorionic and dichorionic twin pregnancies.

METHODS: Unselected twin pregnancies were recruited for this prospective cohort study (N=1,028), which was conducted in eight tertiary referral perinatal centers in Ireland. Perinatal mortality and a composite measure of perinatal morbidity (respiratory distress, necrotizing enterocolitis, hypoxic ischemic encephalopathy, periventricular leukomalacia, or sepsis) were compared between uncomplicated twins that underwent planned preterm delivery compared with monochorionic twins that continued in utero beyond 34 weeks of gestation, and dichorionic twins who continued beyond 36 weeks.

RESULTS: Perinatal outcome data were recorded for 100% of the 1,001 twin pairs that completed the study (n=200 monochorionic and n=801 dichorionic). Overall perinatal mortality was 30 per 1,000 in monochorionic twins and 3.8 per 1,000 among dichorionic twins. The prospective risk of in utero death was 1.5% after 34 weeks of gestation for uncomplicated monochorionic pregnancies, with no deaths among dichorionic twins after 33 weeks. The risk of a composite measure of perinatal morbidity for uncomplicated monochorionic twins fell from 41% (13/32 neonates, 3/6 among elective deliveries) at 34 weeks to 5% (4/84) at 37 weeks ($P<.001$). Among dichorionic twins, the risk of morbidity fell from 4% (2/52) among elective deliveries at 36 weeks to 1% (5/344) in pregnancies continuing to 38 weeks ($P=.231$).

CONCLUSION: Applying a strategy of close fetal surveillance, perinatal morbidity can be minimized by allowing uncomplicated monochorionic pregnancies continue to 37 weeks of gestation and dichorionic twins to 38 weeks. Among monochorionic twins, this approach must be balanced against a 1.5% risk of late in utero death.

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The evolution of advanced reproductive techniques over the past three decades has led to an increase in the incidence of twin pregnancy worldwide. This increase has been observed both in the case of dizygotic and, to a lesser extent, monozygotic twinning.[1–3] In the event of single twin death in a monochorionic pair, there is known to be up to a 30% cumulative risk of co-twin death or of severe neurologic morbidity in the survivor.[4] In light of this risk, some have called for apparently uncomplicated monochorionic gestations to be electively delivered

once the sequelae of preterm delivery are perceived to be low, such as delivery at 32,[5] 34[6] or 36[7,8] weeks of gestation. Such recommendations have all been based on retrospective series that focus solely on the prospective risk of in utero fetal death and provide almost no data on perinatal morbidity. Similarly there are no clear recommendations on the optimum timing of elective delivery of apparently uncomplicated dichorionic twin pairs.

Our objective was to identify the optimum gestational age for elective delivery of apparently uncomplicated monochorionic and dichorionic twin pregnancies by determining the neonatal risk associated with elective delivery at each gestational age in the late-third trimester, and to ascertain the prospective risk of death or severe perinatal morbidity in ongoing pregnancies.

MATERIALS AND METHODS

The prospective ESPRiT Study (Evaluation of Sonographic Predictors of Restricted growth In Twins) 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 were all twin pregnancies presenting to the study centers between 11 and 22 completed weeks of gestation, with both fetuses being alive at the time of enrolment, and with intact membranes. Monoamnionicity, a major structural abnormality in either twin or fetal aneuploidy (either suspected or confirmed) led to exclusion from the study.

All patients meeting inclusion criteria were subjected to a program of intensive fetal surveillance carried out by dedicated trained research ultrasonographers using standardized ultrasound equipment (GE Voluson Expert 730, GE Healthcare). Ultrasound examination included biometry, placental location and number, fetal Doppler measurements, 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 ultrasound 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 of gestation 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. Additionally, when intertwin growth discordance exceeded 20% or if umbilical or middle cerebral arterial Doppler measurements were abnormal, ductus venosus Doppler evaluation was also performed. A quality review system was in place, requiring regular submission by ultrasonographers of images and Doppler traces to a central ultrasound quality-assurance committee.

At each ultrasound examination, the presence or absence of obstetric complications or clinical events was recorded (hypertension, preeclampsia, rupture of membranes, gestational diabetes, antepartum hemorrhage, threatened preterm labor, twin–twin transfusion syndrome, hospital admission and the administration of antenatal corticosteroids for fetal lung maturity).

At a gestational age of 34 0/7 weeks for monochorionic twins and 36 0/7 weeks for dichorionic twins, pregnancies were considered uncomplicated in the setting of fetal growth that was appropriate for gestational age (more than the 10th centile), with normal amniotic fluid volume and normal umbilical artery Doppler evaluation in both twins on predelivery ultrasonography and in the absence of a maternal or fetal indication for delivery. Specifically, cases of prenatally identified twin–twin transfusion syndrome were excluded from this analysis.

Within this cohort of apparently uncomplicated twin pregnancies, subsequent delivery was considered "elective" if birth weights proved to be concordant (less than 20% discordance) and appropriate for gestational age (more than the 10th centile) and in the absence of a maternal or fetal indication for delivery. "Indicated" deliveries refer to deliveries prompted by spontaneous labor, ruptured membranes, maternal or fetal complications such as maternal hypertension, preeclampsia, antepartum hemorrhage, acute twin–twin transfusion syndrome or nonreassuring fetal testing (either cardiotocography, biophysical testing or Doppler indices). Where the birth weight of either twin was less than the 10th centile for gestational age or in the case of birth weight discordance in excess of 20%, delivery was considered indicated for the purpose of this analysis, even if such growth restriction or growth discordance was unanticipated.

All prenatal and ultrasound data were transferred contemporaneously to an ultrasound software system (Viewpoint) and uploaded onto a live web-based central consolidated database. 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 neonatal medical or nursing staff on discharge from the hospital.

Perinatal mortality was defined as death of a fetus or 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 7 days of life. Gestational age at the time of in utero demise was determined by ultrasonography. The perinatal mortality rate was determined using the total number of twin births as a denominator.

Neonatal intensive care unit (NICU) 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 perinatal morbidity included any of the following: 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 less than 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 and was supported by radiographic criteria where available; length of oxygen-dependence was recorded. A diagnosis of neonatal sepsis was made with clinical features confirmed by positive microbiologic cultures. All placentae underwent detailed pathologic examination according to a standardized protocol that included final determination of chorionicity.

Statistical comparisons were performed using the χ^2 test for categorical data and the two-sample t test for continuous data. Where there was evidence of nonnormality, the nonparametric Wilcoxon Rank-sum test was used. Adjustment of perinatal outcomes for gestational age at delivery was incorporated using a Cox proportional hazards model for morbidity outcomes and a linear mixed effects model for continuous outcomes (full cohort, Table 1). For subgroup comparisons of timing of delivery, statistical modeling was not performed and odds-ratios were based on raw frequencies. Analysis of morbidity outcomes was performed on an individual twin basis. The pairing of twins (intra-twin correlation) was appropriately accounted for in the models, using a robust sandwich estimator in the Cox proportional hazards model [9] and random effects in the linear mixed effects model, as implemented in SAS 9.1.

RESULTS

Twin pregnancies recruited during the 2-year study period (N=1,001, May 2007 to May 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 owing to transfer of obstetric care to a nonparticipating center or research staff shortage leading to inability to complete the ultrasonographic surveillance protocol. Perinatal outcome data were recorded on 100% of participants who completed the study. The proportion of twins that was designated as monochorionic and dichorionic by standard ultrasonographic criteria was 20% (205/1,001) and 80% (796/1,001), respectively; chorionicity was reassigned according to placental pathology examination in 17 out of 1,001 cases (1.7%), such that the study comprised 200 monochorionic and 801 dichorionic twin pairs.

Maternal characteristics, obstetric and neonatal morbidities are outlined in Table 1. Mothers of dichorionic twins were, on average, older and, as expected, more likely to have undergone assisted conception. Antenatal obstetric complications were equally prevalent in both monochorionic and dichorionic pregnancies, including gestational hypertension, preeclampsia, gestational diabetes, prelabor preterm rupture of membranes, and antepartum hemorrhage. Twin–twin transfusion syndrome was noted in 10% (20/200) of monochorionic pregnancies and was managed with selective laser photocoagulation of communicating placental vessels in 12 cases. At least one survivor was attained in all cases treated with laser; postprocedure donor demise occurred in 5 out of 12 pregnancies, such that neonatal survival to 28 days of life was recorded for 19 out of 24 (79%) fetuses subjected to fetoscopic laser photocoagulation of the placenta in the prenatal period.

All cases of fetal or neonatal death are described in Table 2. The perinatal mortality rate for normally formed neonates, expressed per total neonates weighing more than 500 g, was 30 per 1,000 (11/380) among monochorionic neonates (95% confidence interval [CI] upper limit 53/1,000) and 3.8 per 1,000 (6/1,583) among dichorionic neonates (95% CI upper limit 10/1,000). Perinatal mortality was corrected for absence of lethal congenital abnormality. The threshold for fetal viability was designated as a minimum gestational age of 24 completed weeks of gestation or

Table 1. Maternal, Obstetric, and Neonatal Characteristics by Chorionicity

	Monochorionic (n=200)	Dichorionic (n=801)	*P*
Maternal characteristics			
Age (y)	31.3	33.0	<.001
Parity (one or more births)	93 (47)	405 (51)	.52
White*	164 (93)	638 (92)	.89
Asian*	5 (3)	24 (3)	
Afro-Caribbean*	7 (4)	25 (4)	
Gestational age (wk) at recruitment	16	16	.51
Assisted conception	6 (3)	227 (28)	<.001
IVF and ICSI	5 (2.5)	185 (23)	
Ovulation induction	1 (<1)	40 (5)	
Intrauterine insemination	0	2 (<1)	
Smoker	21 (11)	93 (12)	.67
Previous cesarean delivery	12 (6)	77 (10)	.13
Pregestational hypertension	0	12 (2)	.08
Pregestational diabetes	4 (2)	8 (1)	.24
Maternal body mass index	25.5±5.0	25.4±4.7	.92
Obstetric characteristics			
Gestational hypertension and preeclampsia	18 (9)	74 (9)	.92
Gestational diabetes	3 (2)	11 (1)	.89
PPROM	5 (3)	21 (3)	.92
Twin–twin transfusion syndrome	20 (10)	NA	NA
Placental abruption	0	5 (0.6)	.26
Antepartum hemorrhage (unclassified)	12 (6)	50 (6)	.89
Placenta previa	2 (1)	7 (0.9)	.87
Obstetric cholestasis	4 (2)	11 (1.4)	.51
	Monochorionic (n=182)†	**Dichorionic (n=788)†**	
Mode of delivery			
Elective cesarean	73 (40)	356 (45)	.21
Emergency prelabor cesarean	27 (15)	73 (9)	.02
Intrapartum cesarean	21 (11.5)	69 (9)	.24
Vaginal delivery × 2 (both twins)	60 (33)	277 (35)	.58
Combined vaginal–cesarean delivery	1 (0.5)	13 (2)	.26

	Monochorionic (n=374)	Dichorionic (n=1,577)	*P* Unadjusted	*P* Adjusted‡
Perinatal morbidity				
Gestational age at delivery (wk)	35.7 (32.9–37.0)	37.1 (35.6–37.9)	<.001	—
Birth weight (g)	2,335 (1,760–2,630)	2,580 (2,205–2,880)	<.001	.58
NICU or SCBU admission	224 (60)	655 (41)	<.001	<.001
NICU or SCBU stay (d)	17 (8–35)	13 (3–21)	<.001	.02
HIE	1 (0.3)	1 (0.1)	.29	.22
PVL	3 (0.8)	3 (0.2)	.07	.07
NEC	4 (1)	7 (0.4)	.17	.11
RDS	85 (23)	194 (12)	<.001	<.001
Sepsis	41 (11)	74 (5)	<.001	<.001
Composite morbidity (HIE, PVL, NEC, RDS, sepsis)	99 (26)	213 (13)	<.001	<.001

IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; PPROM, prelabor preterm rupture of membranes; NA, not applicable; IQR, interquartile range; NICU, neonatal intensive care unit; SCBU, special care baby unit; HIE, hypoxic ischemic encephalopathy; PVL, periventricular leukomalacia; NEC, necrotizing enterocolitis; RDS, respiratory distress syndrome.

Data are mean, n (%), mean±standard deviation, or median (interquartile range) unless otherwise specified.

* Ethnicity missing for 138 patients.

† Mode of delivery data presented for twin pairs with both twins alive at onset of labor or prelabor caesarean delivery.

‡ Adjusted for gestational age at delivery.

a birth weight of at least 500 g. Using this standard definition, previability dual or single in utero fetal death was observed more commonly among monochorionic gestations. Where single monochorionic fetal demise occurred, six of these 11 cases were previable single fetal demises and five occurred after

Table 2. Perinatal Loss: Monochorionic (n=200) and Dichorionic (n=801) Cohorts

	Monochorionic Cohort			Dichorionic Cohort	
Outcome	n=200	Mortality Details	Surviving Co-twin	n=801	Mortality Details
Complete miscarriage	7 (3.5) (GA 15–23 wk)			9 (1.1) (GA 13–22 wk)	
Single IUFD previability	6 (3.0)	19 wk; TTTS; donor IUFD postlaser	Intact	0	NA
		19 wk; TTTS; donor IUFD postlaser	Intact		
		20 wk; TTTS; donor IUFD postlaser	Intact		
		21 wk; TTTS; donor IUFD postlaser	Intact		
		22 wk; recurrent TTTS; postlaser cord ablation	Intact		
		22 wk; IUFD unexplained	Multicystic encephalomalacia		
Single IUFD postviability*	4 (2.0)	28 wk; concordant growth; no evidence of TTTS; unexplained; co-twin delivered at 30 wk; no neurologic sequelae	Intact	1 (0.1)	28 wk; unexplained single IUFD; velamentous cord insertion noted; healthy co-twin delivered at 32 wk
		31 wk; discordant growth and AEDF in umbilical artery from 24 wk; acute TTTS	Intact		
		32 wk; discordant growth; IUFD of larger twin; cord thrombus on postmortem	Intact		
		36 wk; no prenatal ultrasound stigmata of TTTS; "features of recipient TTTS" on path; co-twin delivered at 37 wk; no neurologic sequelae	Intact		
Dual IUFD postviability*	2 (1.0)	26 wk; discordant growth; TTTS 35 wk; acute fetomaternal hemorrhage		1 (0.1)	33 wk; placental abruption
Intrapartum stillbirth*	1 (0.5)	Preterm labor at 23 wk; cesarean delivery for compound presentation; single-twin survival	Intact	0	NA
Neonatal death in one newborn*	0	NA		2 (0.2)	25 wk; preterm labor; neonatal death day 8 (extreme prematurity) 25 wk; trisomy 18
Dual neonatal death*	1 (0.5)	Preterm labor at 24 wk; severe coagulopathy and bilateral grade 4 IVH for both; dual neonatal death day 2 of life.		1 (0.1)	23 wk; extreme prematurity
Dual neonatal survival	179 (90)			787 (98)	
At least one survivor	190 (95)			790 (99)	
Total	200 (100)			801 (100)	

GA, gestational age; IUFD, intrauterine fetal death; TTTS, twin–twin transfusion syndrome; NA, not applicable; AEDF, absent end-diastolic flow; IVH, intraventricular hemorrhage.
Data are n (%).
* Perinatal mortality (postviability fetal and neonatal deaths).

fetal viability (500 g weight or 24 weeks of gestation) was reached. Five of the six previable single fetal demises occurred in the setting of twin–twin transfusion syndrome. Intact neonatal survival with normal neonatal cranial imaging was documented for 10 of 11 co-twins of monochorionic pregnancies in which one twin died in utero, half of whom (5/10) had undergone laser ablation of communicating placental vessels. One twin of a monochorionic pair who was delivered at 28 weeks after unexplained demise of his co-twin at 22 weeks was found to have multicystic encephalomalacia and dysplastic kidneys in the neonatal period.

Figure 1 illustrates the timing of delivery for monochorionic and dichorionic twin pregnancies. The proportion of twins who delivered after 32 completed weeks of gestation was 80% and 93% for monochorionic and dichorionic twin pregnancies, respectively. In the interval between 24 and 28 weeks of gestation, 5% of monochorionic (9/200) and 1.5% of dichorionic (12/801) twins were delivered.

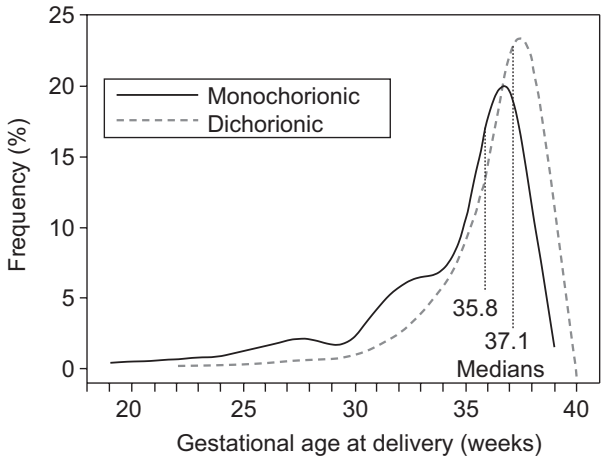

Fig. 1. Distribution of gestational ages at delivery for monochorionic (n=200) and dichorionic (n=801) twin pregnancies.

Breathnach. Delivery of Uncomplicated Twins. Obstet Gynecol 2011.

At a cutoff gestational age of 34 completed weeks, 131 monochorionic twin pregnancies were identified that were not complicated by twin- twin transfusion syndrome and in whom fetal growth was concordant and appropriate for gestational age (more than the 10th centile for gestation). An additional 565 dichorionic twin pairs were identified at 36 completed weeks with neither a maternal nor a fetal indication for delivery. Therefore, 66% (131/200) of monochorionic twins attained a gestational age of 34 weeks with an uncomplicated pregnancy at that point, whereas 71% (565/801) of dichorionic twins were uncomplicated at 36 weeks. Tables 3 and 4 outline, for monochorionic and dichorionic twins respectively, both the neonatal morbidity observed among uncomplicated twins who underwent planned (elective) delivery at each gestational age and the perinatal morbidity recorded among twins whose pregnancies continued.

At 34 completed weeks of gestation, the prospective risk of in utero mortality for either twin of a monochorionic pair in whom twin–twin transfusion syndrome had not evolved and in the absence of ultrasonographic evidence of fetal growth restriction was 1.5% (2/131 pregnancies; or perinatal mortality in 3/262 neonates [1.1%; 95% CI upper limit of 3.6%]). Neonatal morbidity was encountered in either or both twins in three of six uncomplicated monochorionic pairs electively delivered at 34 weeks; the comparative morbidity observed among twin pairs who continued in utero and were delivered either electively or for maternal or fetal indications was 5% (2/44), 9% (7/82) and 5% (4/84) for monochorionic neonates delivered at 35, 36 and 37 weeks of gestation, respectively. Therefore, the risk of a composite measure of perinatal morbidity for uncomplicated monochorionic twins fell from 41% (13/32 neonates,

Table 3. Prospective Risk of Perinatal Mortality and Perinatal Morbidity Among Apparently Uncomplicated Monochorionic Twin Gestations From 34 Weeks of Gestation (n=131 Twin Pregnancies)

Gestational Age (wk)	Prospective Risk of Mortality (per Pregnancy)*	Perinatal Morbidity† Rate (per Neonate) Among Elective‡ Deliveries	Elective Deliveries: Morbidity† Details (per Neonate)	Perinatal Morbidity† Rate (per Neonate) Among Indicated§ Deliveries	Indicated Deliveries: Morbidity† and Mortality Details (per Neonate)	Overall Morbidity Risk† (per Neonate) Among Elective and Indicated Deliveries	NICU Admission Rate (n=256 Neonates)
34–34 6/7	2/131 (1.5) (95% CI upper limit 6.0)	3/6 (50)	RDS (3/6)	10/26 (39)	RDS (6/26) Sepsis (5/26)	13/32 (41) 95% CI upper limit 59)	28/32 (88)
35–35 6/7	2/118 (1.7)	2/14 (14)	Sepsis (2/14)	2/30 (7)	Dual mortality (fetomaternal hemorrhage) (2/30)	2/44 (5)	23/44 (52)
36–36 6/7	1/96 (1.0)	3/26 (12)	RDS (2/26) HIE and sepsis (1/26)	4/56 (7)	RDS (4/56) death ("recipient TTTS") (1/56)	7/82 (9)	27/82 (33)
37–37 6/7	0/49 (0)	3/46 (7)	RDS (3/46) NEC and sepsis (1/46)	1/38 (3)	RDS (1/38)	4/84 (5) (95% CI upper limit 12)	22/84 (26)
38 or more	0/11 (0)	0/16	NA	0/6 (0)	NA	0/22 (0)	2/22 (9)

NICU, neonatal intensive care unit; CI, confidence interval; RDS, respiratory distress syndrome; HIE, hypoxic ischemic encephalopathy; TTTS, twin–twin transfusion syndrome; NEC, necrotizing enterocolitis; NA, not applicable.

Data are n/N (%) unless otherwise specified.

* Prospective risk of mortality per pregnancy refers to the number of perinatal deaths prospectively encountered expressed per total number of pregnancies reaching that gestational week.

† Perinatal morbidity is defined as any of the following: respiratory distress syndrome, necrotizing enterocolitis, hypoxic ischemic encephalopathy, periventricular leukomalacia, sepsis.

‡ Elective delivery refers to scheduled delivery of apparently uncomplicated twins with concordant growth, normal amniotic fluid, and normal Doppler evaluation on predelivery ultrasonography and in the absence of spontaneous labor and ruptured membranes or maternal complications.

§ Indicated deliveries refer to deliveries prompted by spontaneous labor, ruptured membranes, or maternal or fetal complications.

Table 4. Prospective Risk of Perinatal Mortality and Perinatal Morbidity Among Apparently Uncomplicated Dichorionic Twin Gestations From 36 Weeks of Gestation (n=565 Twin Pregnancies)

Gestational Age (wk)	Prospective Risk of Mortality (per Pregnancy)	Perinatal Morbidity Rate (per Neonate) Among Elective* Deliveries	Elective Deliveries: Morbidity† Details (per Neonate)	Perinatal Morbidity Rate (per Neonate) Among Indicated‡ Deliveries	Indicated Deliveries: Morbidity† Details (per Neonate)	Overall Perinatal Morbidity Risk (per Neonate) Among Elective and Indicated Deliveries	NICU Admission Rate (n=1,130 Neonates)
36–36 6/7	0	2/52 (4) (95% CI upper limit 14)	RDS (2/52)	16/202 (8)	RDS (14/202) Sepsis (6/202)	18/254 (7) (95% CI upper limit 11)	92/254 (36)
37–37 6/7	0	7/222 (3)	RDS (7/222)	10/280 (4)	RDS (9/280) Sepsis (3/280) NEC (1/280)	17/502 (3)	114/502 (23)
38–38 6/7	0	3/222 (1)	RDS (2/222) Sepsis (3/222)	2/122 (2)	RDS (2/122) Sepsis (2/122)	5/344 (1) (95% CI upper limit 3.6)	49/344 (14)
39 or more	0	0/20 (0)	NA	0/8 (0)	NA	0/28 (0)	0/20 (0)

NICU, neonatal intensive care unit; CI, confidence interval; RDS, respiratory distress syndrome; NEC, necrotizing enterocolitis; NA, not applicable.
Data are n/N (%) unless otherwise specified.
* Elective deliveries refer to scheduled delivery of apparently uncomplicated twins with concordant growth, normal amniotic fluid, and normal Doppler evaluation on predelivery ultrasonography and in the absence of spontaneous labor and ruptured membranes.
† Perinatal morbidity is defined as any of the following: respiratory distress syndrome, necrotizing enterocolitis, hypoxic ischemic encephalopathy, periventricular leukomalacia, sepsis.
‡ Indicated deliveries refer to deliveries prompted by spontaneous labor, ruptured membranes, or maternal or fetal complications.

3/6 among elective deliveries) at 34 weeks to 5% (4/84) at 37 weeks ($P<.001$). A concomitant fall in the NICU admission rate from 88% (28/32) at 34 weeks to 9% (2/22) at 38 weeks was observed.

Comparing perinatal outcome among elective monochorionic twin deliveries at 34 weeks with that observed in pregnancies that continued beyond this gestation, the odds ratio for adverse perinatal outcome was 13.5 (95% CI 2.5 to 72.4, $P<.001$); however it is acknowledged that the observed increase in perinatal risk is based on a small sample size (n=6). Apparently uncomplicated monochorionic twins delivered at 35–36 weeks, however, continued to demonstrate a higher risk of adverse perinatal outcome, in the order of an odds ratio of 4.9 (95% CI 1.5 to 15.7, $P=.004$) relative to those twins who deliver later. A comparable OR of 5.4 (95% CI 1.5 to 18.9, $P=.004$) was observed at week 36–37 relative to monochorionic twins who delivered after 37 weeks.

Among dichorionic twins there were no deaths, either in utero or ex-utero, after 33 weeks of gestation. Table 4 also reflects a greater risk in morbidity for dichorionic twin pairs delivered electively between 36 and 37 weeks (odds ratio 1.61, 95% CI 0.4 to 7.1, $P=.52$) relative to those delivered after 37 weeks and among electively delivered uncomplicated dichorionic twins delivered at 37–38 weeks relative to after 38 weeks (odds ratio 2.5, 95% CI 0.8 to 7.5, $P=.09$); however, the increased risk of morbidity observed (4% $^{2}/_{52}$ among elective deliveries at 36 weeks compared with 1% $^{5}/_{344}$ in pregnancies continuing to 38 weeks [$P=.231$]) is not on the same scale as the risk demonstrated in monochorionic twins and does not reach statistical significance.

Table 5 outlines the incidence of respiratory distress at each gestational age beyond 34 completed weeks, along with prevalence of in utero corticosteroid exposure. The small number of cases (17) in

Table 5. Respiratory Morbidity and Antenatal Corticosteroid Exposure in Monochorionic and Dichorionic Neonates Delivered After 34 Completed Weeks of Gestation (n=1,650 Neonates)

Gestational Age (wk)	Respiratory Morbidity	Requirement for Assisted Ventilation and CPAP	Steroids Given (at Any Gestation)	Steroid Exposure Among Respiratory Distress Cases	Interval (wk) From Steroid Administration
34–34 6/7 (n=138)	43 (31)	33/43 (77)	69/138 (49)	23/43 (53)	5.7 (3.0–7.3)
35–35 6/7 (n=194)	14 (7)	8/14 (57)	70/194 (36)	9/14 (64)	3.9 (3.0–8.9)
36–36 6/7 (n=338)	23 (7)	8/23 (35)	110/338 (32)	8/23 (35)	9.4 (2.3–10.3)
37–37 6/7 (n=586)	20 (3)	11/20 (55)	140/586 (24)	4/20 (20)	6.7 (5.4–9.9)
38 or more (n=394)	4 (1)	1/4 (25)	78/394 (20)	0/4 (0)	NA

CPAP, continuous positive airway pressure.
Data are n (%), n/N (%), or median (interquartile range).

which chorionicity was re-assigned postpartum delivered at a mean gestational age of 37 weeks (range 33–38 weeks). No adverse perinatal outcome was recorded for any of these cases and analysis of perinatal outcome data did not change with reversion of these cases to their prenatally assigned chorionicity.

DISCUSSION

This study represents a large prospective cohort study of twin pregnancy mortality and neonatal morbidity, with complete perinatal outcome data ascertained beyond 28 days of life on 100% of study participants. Overall mortality and morbidity in this intensively monitored contemporary twin cohort is remarkably low. The perinatal mortality rate, expressed as the number of deaths of neonates who attained a gestational age of at least 24 weeks or weighed in excess of 500 g at birth, either in utero or within the first 7 days of life, expressed per 1,000 total births equated to 30 per 1,000 among monochorionic twins and 3.8 per 1,000 among dichorionic neonates when a single case of lethal congenital anomaly (trisomy 18) was excluded. The definition of perinatal mortality used in our study is the definition used for perinatal audit in this country and serves to reflect the loss of fetuses that have attained potential viability, either by virtue of gestational age or birth weight. It is accepted that there are variations in the definition of perinatal mortality that should be acknowledged when comparing studies. Nonetheless, although the perinatal mortality rate among monochorionic twins is between one half and one quarter of that reported in the literature,[10–12] the dichorionic perinatal mortality rate is lower than that commonly recorded for singleton populations.

Furthermore, for both types of twins, the majority of fetal loss was observed either previability or a gestational age so remote from term that elective preterm delivery would not have been a realistic preventive intervention. It is plausible that the low perinatal mortality rates achieved were a reflection of the frequency of prenatal surveillance (minimum twice-weekly ultrasound surveillance from 24 weeks for dichorionic twins and from 16 weeks for monochorionic pairs. No comparative studies exist that address the issue of twin ultrasound examination regimens targeted at minimizing the risk of perinatal mortality. It is acknowledged, however, that the scanning schedule reported here reflects practice in a research setting and may not be applicable to all clinical settings. Higher fetal death rates are reported in population-based studies where fetal surveillance is not standardized.[13] Nonetheless, it is important to emphasize that this prospective cohort was unselected–this cohort represents the vast majority of twin pregnancies delivered in all eight participating centers during the study period. The only criteria that led to exclusion from recruitment were monoamnionicity, confirmed or suspected major fetal abnormality, rupture of membranes or fetal demise recognized at the time of consideration for enrollment. Although these exclusion criteria have the potential to create an underestimation of early previable twin pregnancy loss, prospective recruitment before 22 0/7 weeks days excluded the possibility of an underestimation of the perinatal mortality rate, for which the denominator is total births (500 g birth weight or 24 weeks of gestational age) and not total pregnancies. Thus the risk of underascertainment of cases of perinatal death was eliminated.

Mode of delivery (presented in Table 1) is commonly perceived to be a factor that influences perinatal outcome among multiple gestations. Yet analysis of perinatal morbidity by mode of delivery in this cohort has demonstrated that neonatal outcome was not influenced by whether a trial or labor was successful or not, and did not differ from the neonatal morbidity observed among twins delivered by planned cesarean. The effect of mode of delivery on perinatal outcome within this cohort forms the subject of an article dedicated to this issue.[14]

Studies to date that have addressed the issue of elective preterm delivery of monochorionic twins as a means of avoiding the risk of single unanticipated fetal death and its potential sequelae for the surviving co-twin of a monochorionic pair have all been retrospective and have included cohorts that span 7–15 years.[5–7] There is an inherent danger in extrapolating conclusions from large cohort studies that span over a decade to the management of twin pregnancies today. The last 15 years have witnessed significant advances in prenatal surveillance, in identification and management of twin–twin transfusion syndrome, and advances in neonatal care.

Respiratory morbidity accounted for the majority of neonatal morbidity and the spectrum of severity was wide but required NICU admission in all cases. Such respiratory morbidity was observed in spite of high rates of antenatal corticosteroid exposure. This observation is consistent with prior studies[15,16] that suggest that in contrast to the well-established benefit of antenatal corticosteroid exposure in singleton pregnancies at risk for preterm delivery, it is possible that antenatal corticosteroids may be less effective in reducing the incidence of respiratory distress syn-

drome in twins. Blickstein and co-investigators have reported observational data indicating that, although a complete course of antenatal corticosteroids reduces the incidence of respiratory distress syndrome in twins, it does not do so to the same extent as in singleton gestations.[17] A pharmacologic rationale for this assertion has been proposed in one study that demonstrated a shorter half-life and enhanced clearance of betamethasone in twin pregnancies compared with singleton pregnancies.[18] Perhaps as a consequence, twins have been found to be more vulnerable to respiratory morbidity than singletons.[15]

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 overall low morbidity and mortality rates recorded among study participants, however, impose limitations on the conclusions that can be drawn relating to the minimizing of adverse perinatal outcome. Furthermore, this was a highly compliant study population, making the degree to which the study surveillance protocol affected perinatal morbidity impossible to judge. Nonetheless, this study is unique in attempting to address the balance of in utero compared with ex utero risk.

For monochorionic twins, the motivation for elective preterm delivery is to eliminate the risk of unanticipated in utero fetal demise at a later gestational age. This study quantifies that risk at 1.5% or 1.7% at 34 or 35 weeks of gestation respectively. Although elective delivery at 34 or 35 weeks abolishes that specific risk, that decision incurs a cost of neonatal morbidity that translates into an 88% NICU admission rate at 34 weeks, falling to 9% at 38 weeks. Nonetheless, although the absolute risk of unanticipated in utero mortality may be perceived to be low, the consequences of late fetal death in a monochorionic twin pregnancy are sufficiently devastating that patients may opt to accept a perinatal morbidity risk that is predominantly respiratory and transient in the interests of eliminating the risk of perinatal death and its associated risk of co-twin death or severe neurologic sequelae.

In the case of dichorionic twins, the risk of in utero demise appears to be almost negligible in the setting of intensive ultrasonographic fetal surveillance, and the absence of interdependence of placental vasculature confers a lesser threat to the pregnancy in its entirety. A composite measure of perinatal morbidity, however, is seen to fall steadily from 7% at 36 weeks to 1% at 38 weeks, such that the decision to proceed with elective preterm delivery of an appropriately grown and concordant dichorionic twin pregnancy before 38 weeks should be taken only after data such as that gleaned from this study is shared with patients.

Appropriate selection of timing of delivery for both monochorionic and dichorionic twin pregnancies is a matter not just of considering the prospective risk of in utero demise, but acknowledging the dynamic balance that exists between in utero (fetal) risk and ex-utero (neonatal) risk. Such consideration should allow empowerment of parents toward more informed decision-making when balancing the risks and benefits of elective preterm delivery.

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