The Natural Course of Monochorionic and Dichorionic Twin Pregnancies: A Historical Cohort

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Current early diagnosis, surveillance and intervention options make it hard to determine the natural course of twin pregnancies, especially regarding spontaneous preterm delivery and perinatal mortality. We studied the natural course in monochorionic (MC) and dichorionic (DC) twin pregnancies in a historical cohort. Twin pregnancies were studied in a unique database of 651 twin pairs born in the period 1907 to 1938. We examined the effect of chorionicity on gestational age, birthweight, perinatal mortality, intertwin birthweight differences, the incidence of preeclampsia and maternal mortality. Perinatal mortality was 27.7% for MC and 15.8% for DC twins ($p < .001$). Gestational age and birthweight were stronger predictors of perinatal mortality than chorionicity. Perinatal outcome was poorer for the second twin, especially in DC twins. Delivery before 37 weeks of gestation occurred more often in MC twin pregnancies (48.8% compared to 33.3% in DC twin pregnancies). DC twins were on average 288 g (95% confidence interval 201–376) heavier than MC twins. Severe birthweight discordancy occurred equally in MC and DC twins (18.1%). However, if present, mortality was only increased in MC twins. The birthweight of girls was not affected by the presence of a male co-twin. In this historical cohort MC twin pregnancies had a higher perinatal mortality, caused by a high incidence of low birthweight mainly due to preterm delivery. Mortality did not differ in deliveries after 31 weeks of gestation, which is in contrast to recent data. Apparently, modern obstetrics is more effective in reducing mortality in DC twins.

Following widespread application of assisted reproductive technology modalities, the incidence of twin gestations has increased markedly (Luke, 1994). In the Netherlands, the number of born twins was 13.4/1000 births in the early 20th century, whereas at the end of the 20th century there were 18.1 twins per 1000 births (CBS, 2002).

Twins are at higher risk for preterm delivery, low birthweight, pregnancy-induced hypertension and neonatal, postnatal and infant death compared to singletons (Powers & Kiely, 1994). In order to design potential strategies to reduce this high risk, more knowledge is needed about the natural course of twin pregnancies. Nowadays, fetal surveillance, medication and a high cesarean section rate may influence outcome of twin pregnancies.

We were able to explore the natural course of twin pregnancies in a unique database of 651 twin pairs born in the Netherlands between 1907 and 1938. Chorionicity was carefully ascertained and documented post partum. By that time, there was no ultrasound screening or fetal monitoring and hardly any tools to intervene. We were specifically interested in differences between monochorionic (MC) and dichorionic (DC) pregnancies, since MC twins are generally believed to be at a higher risk as compared to DC pregnancies (Hatkar & Bhide, 1999; Sebire et al., 1997; Snijder &Wladimiroff, 1998; Victoria et al., 2001), due to vascular anastomoses in the placenta. A number of studies have been published concerning this subject, possibly leading to intensified surveillance of monochorionic twin pregnancies, which currently makes comparison with DC pregnancies difficult (Minakami et al., 1999; Sebire et al., 1997; Wenstrom et al., 1992). Again, this historical natural course design circumvents these problems.

Material and Methods

Between 1907 and 1938 the Dutch gynecologist De Snoo and his registrar Bär recorded a total of 651 twin pregnancies in Utrecht, Rotterdam and surrounding areas. In a standardized manner they recorded several data concerning chorionicity, perinatal mortality and general pregnancy characteristics. Chorionicity was classified as DC or MC according to the number of chorion and amnion layers in the placenta.

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Table 1

Characteristics of Twin Pregnancies Between 1907 and 1938 in the Netherlands According to Chorionicity

	Monochorionic twin pregnancies	Dichorionic twin pregnancies
Number of pregnancies	164 (27.2%)	439 (72.8%)
Median age of mother in years (range)[1]	29 (19–43 years)	30 (17–45 years)
Median parity of mother (range)	2 (1–13 children)	3 (1–21children)
Median gestational age in weeks (range)	37 (22–40 weeks)	38 (20–42 weeks)
Sex distribution	49.5% boys, 50.5% girls	54.4% boys, 45.6% girls
Preeclampsia[2]	13 (7.9%)	22 (5.0%)
Eclampsia	4 (2.4%)	8 (1.8%)
Delivery before 37 weeks of gestation	78 (47.6%)	141 (32.1%)
Delivery before 32 weeks of gestation	31 (18.9%)	37 (8.4%)
Mean placental weight (*SD*)[3]	877 g (263)	982 g (231)

Note: [1]One missing value in monochorionic (MC) twin pregnancies, leaving 163 MC pregnancies to be analyzed and 11 missing values in dichorionic (DC) pregnancies, leaving 428 pregnancies.

[2]12 missing values in MC pregnancies, leaving 152 MC pregnancies to be analyzed and 40 missing values in DC twin pregnancies, leaving 399 pregnancies to be analyzed.

[3]In 128 MC and 367 DC twin pregnancies placental weight is known (108 missing values).

Gestational age was calculated from the first day of the last menstrual period. According to the definition of perinatal mortality of the World Health Organization (WHO, 2005), all fetuses smaller than 500 g (n = 21) and all fetuses delivered before 20 weeks of gestation (n = 31) were excluded. Macerated children (with a birthweight of greater than 500 g) were included in the overall perinatal mortality rate. However, for the calculation of perinatal mortality per gestational age, macerated infants with a birthweight under the 10th percentile (n = 23) were excluded since time of death could not be determined. We assumed that a macerated child with a birthweight above the 10th percentile may have died in the week of delivery. The Dutch birthweight charts used in this study come from an Amsterdam population from the years 1931 to 1965 (Kloosterman, 1970). Also children with unknown chorionicity (n = 48) were excluded, thus leaving 1179 children to be analyzed.

Perinatal mortality was defined as the death of an infant with a birthweight over 500 g within 1 week of delivery, including stillbirth. Perinatal mortality rates were also calculated for each week of gestation. This was defined as the number of infants that died divided by total number of infants born that week, expressed as a percentage.

Preterm delivery was defined as delivery before 37 weeks of gestation and *very preterm delivery* as delivery before 32 weeks. Low birthweight was expressed as a birthweight of less than 1500 g. The intertwin difference in weight was expressed as a percentage of the weight of the heaviest twin. There is an ongoing controversy whether the presence of a male twin affects the birthweight of his female co-twin (Blumrosen et al., 2002; Glinianaia et al., 1998). Therefore we compared birthweight of females in unlike-sexed twin pairs with those of female twin pairs. Placental weight included the chorion and amnion layers of the placenta.

Preeclampsia was defined as hypertension (systolic blood pressure greater than 160 mm Hg) in combination with albuminuria. At that time, diastolic blood pressure was almost never recorded in contrast to systolic blood pressure, which was carefully documented. The presence of proteins in urine was determined by a cooking test (according to Bang), used frequently in the early 20th century to assess albuminuria. Eclampsia, as well as maternal death, was distinctively recorded by the treating physician.

The data were analyzed with SPSS 12.0 (SPSS Inc., 2003). To test whether categorical variables differed between MC and DC twins we used a chi-square test. Differences between continuous variables were tested according to chorionicity by means of an independent sample t test or a Mann-Whitney U test, whenever appropriate. Possible confounders were corrected for with logistic and linear regression. Logistic regression was also used to evaluate the relation between birthweight (differences) and perinatal mortality. Kaplan-Meier analysis was used to estimate the cumulative survival. Statistical significance was based on two-sided tests with a cut-off level of .05.

Results

Baseline characteristics of the study population are shown in Table 1. The number of DC twin pregnancies was almost three times that of MC twin pregnancies. Nine MC twin pregnancies were monoamniotic, of which three children died and 15 survived. MC twins did not substantially differ from DC twins in the age of the mother or her parity at birth or gender distribution. The median gestation was 1 week longer in DC twins and the mean birthweight was substantially higher in the DC group. DC twins were an average of 288 g (95% confidence interval [CI] 201–376) heavier than MC twins. Exclusion of stillbirths did not influence this (data not shown).

Table 2

Perinatal Mortality in Mono- and Dichorionic Twins Born Between 1907 and 1938 in the Netherlands According to Gestational Age

Gestational age in weeks	Monochorionic twins					Dichorionic twins				
	No. of pregnancies	Death of one infant per pregnancy (*n*)	Death of both infants per pregnancy (*n*)	No. of infants born[1]	No. of deceased infants (*n*)	No. of pregnancies	Death of one infant per pregnancy (*n*)	Death of both infants per pregnancy (*n*)	No. of infants born[1]	No. of deceased infants (*n*)
20–25	9	0	9 (100%)	18	18 (100%)	9	0	9 (100%)	18	18 (100%)
26–29	12	0	12 (100%)	20	20 (100%)	17	1 (5.9%)	16 (94.1%)	34	33 (97.1%)
30–31	10	2 (20%)	6 (60%)	20	14 (70%)	11	2 (18.2%)	6 (54.5%)	22	14 (63.4%)
32–33	10	4 (40%)	1 (10%)	19	5 (26.3%)	22	6 (27.3%)	5 (22.7%)	42	13 (31%)
34–35	15	1 (6.7%)	2 (13.3%)	28	3 (10.7%)	34	6 (17.6%)	4 (11.8%)	67	13 (19.4%)
36–37	39	6 (15.4%)	4 (10.3%)	73	10 (13.7%)	87	10 (11.5%)	4 (4.6%)	174	18 (10.3%)
38–39	28	2 (7.1%)	1 (3.6%)	53	1 (1.9%)	66	6 (9.1%)	1 (1.5%)	131	7 (5.3%)
> 40	41	2 (4.9%)	2 (4.9%)	81	6 (7.4%)	193	17 (8.8%)	1 (0.5%)	379	13 (3.4%)
Total	164			312		439			867	

Note: [1] Number of infants born per gestational age can be lower than expected from the number of pregnancies due to exclusion of macerated infants with a birthweight of less than 10th percentile.

Adjustment for gestational age largely attenuated this relation, although DC twins were still significantly heavier than MC twins (138 g, 95% CI 132–144). The mean birthweight of females in the presence of a male co-twin was not significantly higher than mean birthweight of females in same-sex pairs (mean birthweight of 2402 g in unlike-sexed twin pairs compared to 2338 g if both infants were female).

The incidence of stillbirths in MC twins was 2.2% compared to 1.5% in DC twins (p = .49). Overall perinatal mortality was 19.1%. Risk of perinatal death was 27.7% for MC and 15.8% for DC twin pregnancies (p < .001). Figure 1 shows the cumulative survival curve for both MC and DC pregnancies, starting at 20 weeks of gestation. Throughout pregnancy, perinatal mortality was significantly higher in MC pregnancies (log rank test, p = .01). Table 2 shows the perinatal mortality of MC and DC twins according to gestational week. Although perinatal mortality was higher in MC pregnancies, it is remarkable that perinatal death was somewhat higher in DC twins between 32 and 35 weeks of gestation. For both chorionicities there was still a considerable perinatal mortality in term pregnancies, 6.5% and 4.9% respectively.

Pregnancy outcomes are also shown in Table 3. The risk of perinatal death was two (95% CI 1.50–2.74) times higher in MC twin pregnancies than in DC twin pregnancies. Birthweight discordancy hardly explained this relation, but adjustment for gestational age and birthweight largely attenuated the association between chorionicity and perinatal mortality (odds ratio [OR] 0.95, 95% CI 0.60–1.51). Gestational age and birthweight were stronger predictors of perinatal mortality than chorionicity. Perinatal outcome was poorer for Twin B and this was significant for DC twins, also after adjustment for differences in birthweight.

Preterm delivery (before 37 weeks of gestation) occurred in 48.8% of MC pregnancies and in 33.3% of DC pregnancies (p < .001). The proportion of twins delivering 'very preterm' (before 32 weeks) was also higher in MC than in DC twins (22.6% and 10.1%, respectively; p < .001). Twenty-six per cent of MC twins born before 37 weeks of gestation had a very low birthweight (less than 1500 g), as compared to 24.5% in DC twins (p = .73). A birthweight of less than 1500 g was strongly associated with perinatal death (91 out of 115 children; 79%), in contrast to 146 out of 1095 children (13.3%) who died with a birthweight of 1500 g or more. The risk of perinatal mortality was not influenced by differences in birthweight between both infants. However, in the presence of severe birthweight discordancy

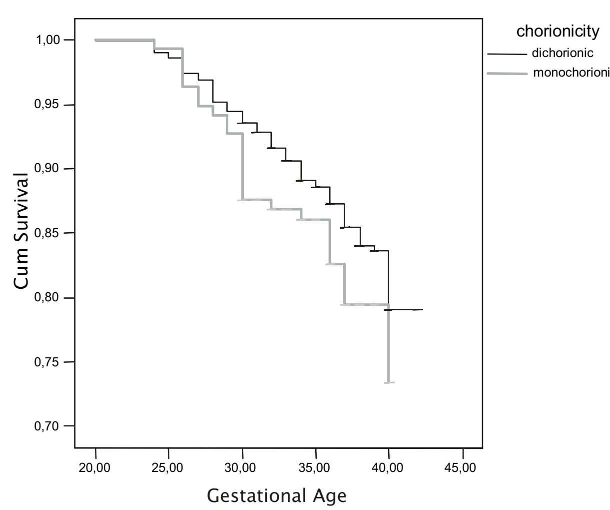

Figure 1

Survival plot for monochorionic (grey) and dichorionic (black) twins born between 1907 and 1938 in the Netherlands (Kaplan Meier).

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Table 3

The Association of Chorionicity and Adverse Pregnancy Outcome in Twins Born Between 1907 and 1938 in the Netherlands

	Monochorionic twins		OR (95% CI)	Dichorionic twins		OR (95% CI)
	Twin A	Twin B		Twin A	Twin B	
Number of children	157	155		432	435	
Mean birthweight after exclusion of still births (*SD*)[1]	2219 g (638)	2170 g (624)		2490 g (665)	2461 g (655)	
Overall perinatal mortality	26.4%	29.0%	1.14 (0.70–1.86)	13.0%	18.6%	1.53 (1.06–2.21)
			1.20 (0.69–2.10)*			1.46 (0.99–2.15)*
Perinatal mortality after exclusion of macerated fetuses with birthweight less than 10th percentile	23.6%	25.8%	1.13 (0.67–1.89)	12.0%	17.7%	1.57 (1.08–2.30)
			1.18 (0.64–2.16)*			1.50 (1.00–2.25)*
Stillbirths	3.8%	0.6%	0.16 (0.02–1.37)	1.6%	1.4%	0.85 (0.28–2.55)

Note: [1] Exclusion of 20 stillbirths, leaving 305 monochorionic twins (151 Twin A and 154 Twin B) and 854 dichorionic twins (425 Twin A and 429 Twin B).

* Adjusted for birthweight differences between Twin A and Twin B.

(greater than 20%) perinatal mortality rates were higher for MC than for DC twins (33.3% and 15.7%, respectively), despite the equal occurrence of these weight differences in both chorionicities (18.1%).

The incidence of eclampsia in MC pregnancies was 2.4% (4 of 164) and in DC pregnancies 1.8% (8 of 439). Two women died as a result of the eclampsia. Thirteen out of 164 (7.9%) women carrying MC pregnancies suffered from preeclampsia, compared to 22 out of 439 (5.0%) women with DC pregnancies. Perinatal mortality was higher in MC twin pregnancies complicated by preeclampsia than in DC twin pregnancies, 33.3% and 12.2% respectively ($p = .07$). Mean placental weight was lower in the presence of preeclampsia (929 g as compared to 970 g in women without preeclampsia), independent of chorionicity.

Nine women (1.5%) died during delivery or in the perinatal period. Three of them had a MC pregnancy (1.8%) and six a DC pregnancy (1.4%). Four deaths were related to infections (encephalitis, tuberculosis and pneumonia), three to thromboembolic events and two to eclampsia.

Discussion

Our study showed a higher perinatal mortality in MC twin pregnancies than in DC twin pregnancies — an association that could largely be ascribed to differences in gestational age and birthweight, but not to birthweight discordancy. It seemed that the association between chorionicity and perinatal mortality was strongest in infants born before 32 weeks of gestation. Preterm delivery occurred more frequently in MC twins. The strongest determinants of perinatal mortality were birthweight and gestational age. Despite an equal occurrence of severe birthweight discordancy in MC and DC twins, such a weight discordancy was related to impaired outcome only in MC twins.

The limitation of this study was that time of intrauterine death could not be documented because there was no ultrasound. Fifty-four children were born macerated. Because of their uncertain gestational age at time of intrauterine demise, we could have excluded them from our data. However, we assumed that a macerated child with a birthweight above the 10th percentile could have died in the week of delivery. We therefore decided to exclude only the 24 macerated fetuses with a birthweight under the 10th percentile when analyzing perinatal mortality per gestational age, which could have biased our data.

We decided not to exclude nine monoamniotic pregnancies. Monoamniotic twins are at increased risk of preterm delivery and fetal death, primarily due to cord accidents and cord entanglement (Allen et al., 2001). Therefore outcome of monoamniotic twins could have distorted death rates of the MC group, but it appeared that exclusion of these pregnancies from our database did not influence the results.

Another limitation of this study concerned gestational age, which was only based on the presumed first day of the last menstrual period. However, this is unlikely to have caused a bias when comparing MC and DC pregnancies. Our data may be extrapolated to a total twin population since it was derived from two areas in the Netherlands and included both home and hospital deliveries.

Because of the historical nature of this study, we cannot compare our results with modern literature. Unfortunately, most of the older literature on perinatal mortality in twin pregnancies did not distinguish mortality according to chorionicity. In 1949 Potter and Fuller published a study of multiple pregnancies delivered at the Chicago Lying-in Hospital (Potter & Fuller, 1949). They found that mortality was slightly higher for twins with MC placentas (13.2%) than for those with DC placentas (9.6%).

It is an important and unsolved issue as to when pregnancy should be terminated in the case of MC or DC twin pregnancy. We therefore studied the relation between perinatal survival rates and gestational age.

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To our surprise there were no large differences in survival for MC and DC twins born after 32 weeks of gestation, with a tendency even of a higher mortality in the DC ones between 32 and 35 weeks. In term pregnancies, the risks of perinatal death were still considerable and identical between both groups (6.5% and 4.9%, respectively). Nowadays perinatal death in term DC twin pregnancies is relatively low (0.5% to 4.5%; Bleker & Oosting, 1997; Derks et al., 2003; Sebire et al., 1997; Stroeken et al., 2005), but death in MC twins is still increased (2.0% to 6.8%). So, modern surveillance and intervention seem efficient regarding DC twins, but not as to MC twins. Elective delivery of uncomplicated DC twin pregnancies at 36 to 37 weeks of gestation does not seem to improve the outcome (Udom-Rice et al., 2000). However, one may consider delivering MC twins at around 37 weeks, giving their increased mortality thereafter and the present incapability to identify the ones at real risk (Barigye et al., 2005; Hartley et al., 2001).

There are a number of recent publications indicating that the presence of a male twin affects the birthweight of his female co-twin (Blumrosen et al., 2002; Glinianaia et al., 1998). This increase in mean birthweight of females in unlike-sex pairs could be explained by the transport of the sex hormones of one fetus to another. Androgens may influence intrauterine growth in female co-twins in unlike-sex twin pairs (Glinianaia et al., 1998). We did not find a tendency for birthweight in females to be influenced by the presence of a male co-twin. This is in agreement with two other studies (Goldman et al., 2003; Orlebeke et al., 1993).

Our data support that preeclampsia is an important cause of perinatal mortality, especially in MC twins. However, due to the limited number of MC twin pregnancies complicated by preeclampsia, no significant differences in perinatal mortality were observed.

In conclusion, this historical cohort shows that MC twin pregnancies appear to carry more risks, mainly due to a high incidence of preterm delivery and low birthweight. Nowadays, ultrasound screening, fetal monitoring and possible intervention options increase survival rates of twin pregnancies. This is especially the case in DC twins. Improvement in the outcome of (term) MC twins has been limited and this needs further investigation.

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