THE JOURNAL OF
Obstetrics and Gynaecology Research

doi:10.1111/jog.12258 J. Obstet. Gynaecol. Res. Vol. 40, No. 3: 711–717, March 2014

Prospective study of the MD-twin score for antepartum evaluation of monochorionic diamniotic twins and its correlation with perinatal outcomes

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Abstract

Aim: To assess the outcome of monochorionic diamniotic (MD) twins with the aid of the MD-twin score.

Methods: We enrolled 112 MD-twin women in a tertiary perinatal center from 1997 to 2009. The MD-twin score was prospectively applied once per week to women who did not have twin-to-twin transfusion syndrome (TTTS) after 26 weeks of gestation. The MD-twin score consists of five variables: (i) fetal weight discordance; (ii) amniotic fluid discordance; (iii) hydrops fetalis; (iv) umbilical cord insertion; and (v) fetal heart rate monitoring. Normal was assigned a value of 0, abnormal was assigned 1, and total score was used for evaluation. Women with scores of 2 at 26 weeks gestation were managed expectantly until the score reached 3. Outcome measures were fetal death, neonatal death and neurological sequelae. The incidence of poor outcome according to score was investigated. The characteristics of MD twins with poor outcome were investigated.

Results: MD-twin scores were applied to 90 women. Among them, 79 had scores of 2 or less and all had good outcomes. There were 11 women with a score of 3, four of whom had adverse outcome for at least one twin. Neonates born to women with scores of 0–2 had good outcomes without respect to birthweight percentile, while neonates with scores of 3 had poor outcomes when their birthweight percentile was less than the third percentile.

Conclusion: The MD-twin score is applicable to 90% of MD twins without TTTS. An MD-twin score of 2 is reassuring, while a score of 3 indicates increased risks for adverse outcome.

Key words: antepartum surveillance, monochorionic diamniotic twin neurological deficit, perinatal outcome.

Introduction

Compared to dichorionic twins, monochorionic diamniotic (MD) twins have disproportionately higher rates of perinatal mortality and morbidity.[1–4] One cause of this is the unique problem of twin-to-twin transfusion syndrome (TTTS), which develops in 10–20% of MD twins due to abnormal placental vascular architectures. In a recent randomized trial of severe TTTS diagnosed before 26 weeks of gestation, fetoscopic laser surgery resulted in a higher survival rate (54%) and less neurological sequelae in survivors at 6 years of age (18%).[5] Despite the introduction of fetoscopic laser surgery, several problems persist. For example, MD twins incur a higher incidence of cerebral injury, primarily of antenatal origin.[6,7] Even at term, unexpected

Received: January 29 2013.
Accepted: August 1 2013.
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Conflict of interest: All authors disclose no financial or personal relationship with other people or organizations that could inappropriately influence (bias) the present work, including employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

fetal demise occurs.[8] Compared to dichorionic twins, MD twins have a higher risk of perinatal morbidity even after the exclusion of complications unique to monochorionic placentation.[9] Furthermore, fetal death after 32 weeks of gestation was significantly higher in MD twins than in dichorionic twins, in which antepartum fetal condition was reassuring in most cases.[10]

Recently, we introduced a new antepartum scoring method, the MD-twin score, using five variables: (i) fetal weight discordance; (ii) amniotic fluid discordance; (iii) hydrops fetalis; (iv) umbilical cord insertion; and (v) fetal heart rate monitoring. Each variable was assigned a value of 0 if normal and 1 if abnormal, yielding scores from 0 (all normal) to 5 (all abnormal). We showed its effectiveness in a retrospective study. When we chose a score of 3 as the cut-off point for a poor outcome, the likelihood ratio became the highest of any single variable or any combination of variables.[11]

Following our previous results, we organized this prospective study to: (i) observe temporal changes in MD-twin score in advancing gestational age; (ii) to clarify the effectiveness of MD-twin score for improving infant mortality and neurological outcome; and (iii) to clarify the limitations of the MD-twin score.

Methods

A prospective, one-arm, cohort study was conducted in a single tertiary perinatal center at the University of Miyazaki Hospital, from January 1997 to December 2009. The current research project was approved by our department's ethics committee. It conforms to the provisions of the Declaration of Helsinki and a written informed consent was obtained from all women involved.

The MD-twin score consists of five variables.[11] Briefly, weight discordance was defined as 25% or more of the heavier twin by ultrasonographic estimation. Amniotic fluid discordance was determined by oligohydramnios (vertical maximum pocket, ≤2 cm) in one, or hydramnios (≥8 cm) in the other. Abnormal cord insertion was defined as either marginal (<2 cm from the edge) or velamentous. Abnormal FHR patterns were as follows: occasional late decelerations, occasional severe variable decelerations, sinusoidal pattern and loss of variability. However, ominous FHR patterns such as recurrent late decelerations, recurrent variable decelerations and prolonged decelerations with absent baseline variability were not included in the scoring system because by themselves they were indications for delivery when fetuses became viable.

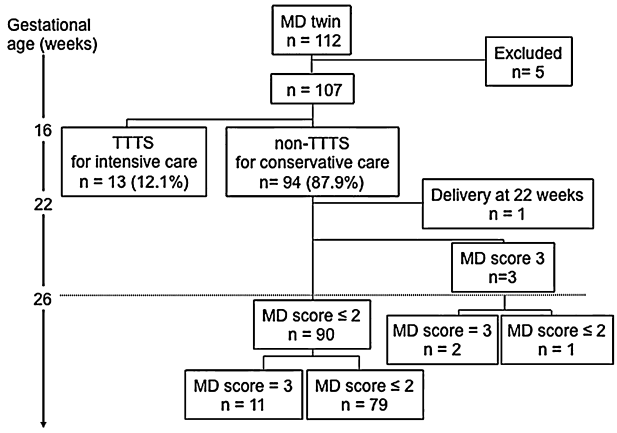

Figure 1 Management flow diagram in the present study.

Each variable was assigned a value of 0 if normal and 1 if abnormal, yielding a range of total scores from 0 (all normal) to 5 (all abnormal). The MD-twin score was evaluated weekly if the score was 0 or 1, and twice per week if the score was 2.

The management diagram is presented in Figure 1. MD twins were diagnosed using ultrasonography during the first trimester. Before 22 weeks of gestation, they were classified into TTTS and non-TTTS according to amniotic fluid discordance of the maximum vertical pocket (2 cm and 8 cm, respectively).[12] Women with TTTS were managed with intensive care including amnioreduction and fetoscopic laser surgery as indicated.

For non-TTTS women, management plans were determined according to gestational ages. During 22–26 weeks of gestation, usual care was provided, including fetal heart rate monitoring (1/day), ultrasonography (1/week) for fetal growth, amniotic fluid evaluation and biophysical profile scoring (1/week). The MD-twin score was measured but not used for clinical decision-making during this period because of borderline viability. When the score reached 3, they were individualized, and usually managed expectantly until ominous signs appeared.

At 26 weeks or after, we applied the MD-twin score, and when women reached a score of 3 for the first time, we terminated the pregnancy and intensive neonatal care was given. If the score stayed at 2 or lower until term (≥37 weeks), delivery was determined by routine obstetric indications such as non-reassuring fetal status, labor onset and term.

If premature labor occurred, tocolytic agents such as β-agonist or magnesium sulfate were used. A cesarean

section was performed according to the following criteria: MD-twin score of 3, previous cesarean section, non-vertex presentation in one twin and other obstetric indications. Chorionicity was confirmed after delivery by histopathological examination of the placenta. A light-for-date infant was defined as having a birthweight below the 10th percentile for gestational age according to the standard Japanese birthweight curves.[13]

Outcome measures were fetal death, neonatal death, infant death and neurological sequelae. The neurological development of all infants was followed and assessed at 3 years old by pediatric neurologists. Motor and mental development was assessed using the Enjoji Scale of Infant Development,[14] a standardized measure of development widely used in Japan.

The presence of twin anemia–polycythemia sequence (TAPS) was also evaluated after birth based on postnatal criteria, which were defined by the presence of anemia (hemoglobin, 11 g/dL) in one twin and polycythemia (hemoglobin, 20 g/dL) in the other twin at birth without signs of TTTS.[15]

Categorical variables, such as perinatal outcome, were analyzed with the χ^2-test. Interval variables such as gestational age and birthweight were analyzed with the Mann–Whitney *U*-test. Statistical analyses were conducted using StatView software for Mac (SAS Institute). $P < 0.05$ were considered significant. Data are shown as mean ± standard deviation.

Results

One hundred and twelve women were enrolled (Fig. 1). Five women were excluded due to abortion ($n = 3$), acardia ($n = 1$) and anencephaly ($n = 1$). Of the remaining 107 women, 13 (12%) were diagnosed as having TTTS and received intensive care. Thus, 94 (88%) women were eligible for the prospective cohort study. Another four women were excluded; one delivered at 22 weeks and three attained a score of 3 before 26 weeks. Finally, the remaining 90 women (80% of the enrolled 112 women) had MD twin scores of 0–2 at 26 weeks of gestation and were managed prospectively with the current protocol.

Maternal characteristics of the 90 women are presented (Table 1). Cesarean birth rate was 87%. Average gestational age at delivery was 34 weeks. Major obstetric complications included anemia (76%), hypertension (9%) and gestational diabetes mellitus (6%).

The MD-twin score varied between 0 ($n = 26$), 1 ($n = 32$), 2 ($n = 21$) and 3 ($n = 11$) (Table 2). Seventy-nine women with scores of 0–2 delivered at 35 ± 2.1 weeks with all infants neurologically normal. Poor outcome occurred exclusively in the remaining 11 with scores of 3. Incidence of poor outcome was significantly higher in those who scored 3 than in those who scored 0–2 (4/11 vs 0/79, $P < 0.01$, χ^2-test). Women with scores of 3 delivered more prematurely at 31 ± 2.7 weeks ($P < 0.01$, Mann–Whitney *U*-test). Poor outcome occurred in only two combinations of the variables

Table 1 Maternal characteristics of the 90 women

No. of pregnancies	90
Maternal age (years), mean ± SD	29.4 ± 5.4
Nulliparity, *n* (%)	50 (55.6)
Cesarean section, *n* (%)	78 (86.7)
Gestational age at delivery (weeks), mean ± SD	34.8 ± 2.6
Anemia, *n* (%)	76 (84.4)
Hypertension in pregnancy, *n* (%)	8 (8.9)
Gestational diabetes, *n* (%)	5 (5.6)

SD, standard deviation.

Table 2 Combination of variables and prognosis

MD-twin score (*n*)	BW	AF	CI	FHR	HF	No. of abnormal pairs/total
0 (26)	0	0	0	0	0	0/26
	1	0	0	0	0	0/1
1 (32)	0	1	0	0	0	0/7
	0	0	1	0	0	0/20
	0	0	0	1	0	0/4
	0	0	0	0	1	—
	1	1	0	0	0	0/2
	1	0	1	0	0	0/5
	1	0	0	1	0	—
	1	0	0	0	1	—
2 (21)	0	1	1	0	0	0/4
	0	1	0	1	0	0/1
	0	1	0	0	1	—
	0	0	1	1	0	0/9
	0	0	1	0	1	—
	0	0	0	1	1	—
	1	1	1	0	0	1/3
	1	1	0	1	0	—
	1	1	0	0	1	—
	1	0	1	1	0	3/6
3 (11)	1	0	1	0	1	0/1
	1	0	0	1	1	—
	0	1	1	1	0	0/1
	0	1	1	0	1	—
	0	1	0	1	1	—
	0	0	1	1	1	—

0, normal variable; 1, abnormal variable; AF, amniotic-fluid volume discordance; BW, birthweight discordance; CI, cord insertion; FHR, fetal-heart-rate monitoring; HF, hydrops fetalis.

Table 3 Details of four sets with poor outcome

No.	Abnormal variables	GA (weeks + days)	BW (g)	BW percentile	Hb (g/dL)	Neonatal complication	Perinatal outcome
1	BWD, CI,	30 + 3	1177	3–10	10.7	n.p	Normal
	FHR		1605	>10	12.8	Hypovolemic shock	CP
2	BWD, CI,	32 + 3	1368	<3	15.6	n.p	CP
	FHR		1798	>10	15.7	n.p	Normal
3	BWD, CI,	30 + 4	1058	<3	16.2	n.p	MR
	FHR		1344	>10	18.7	n.p	Normal
4	BWD, CI,	27 + 1	530	<3	14.5	Cardiac failure	Death (295 days of life)
	AF		1048	>10	21.8	n.p	Normal

AF, amniotic-fluid volume discordance; BW, birthweight; BWD, birthweight discordance; CI, cord insertion; CP, cerebral palsy; FHR, fetal heart rate; GA, gestational age; Hb, hemoglobin at birth; MR, mental retardation; n.p, nothing particular.

(Tables 2,3). In this study, there were no MD twins with TAPS, even in the cases of poor outcome (Table 3).

We evaluated the accuracy of ultrasonographic diagnosis in cord insertion. In the women with MD twin score of 2 or less, there was overestimation in one case and under estimation in three cases. As a whole, 96% of cases with abnormal cord insertion were correctly diagnosed.

Women with poor perinatal outcomes were summarized (Table 3). In case 1, a larger twin with normal cranial ultrasonographic findings urinated excessively, resulting in hypovolemic shock at 8 h of life, and leading to cerebral palsy. Cases 2 and 3 each had a healthy infant and a severe intrauterine growth restriction (IUGR) infant (<3rd percentile) with neurological damage at delivery. In case 4, a premature IUGR infant had focal intestinal perforation and chronic lung disease and died at 10 months. Thus, poor outcome was associated with neonatal circulatory collapse ($n = 1$) and severe premature IUGR ($n = 3$).

Because severe premature IUGR was associated with poor outcome in the present study, we also investigated the effect of IUGR on perinatal outcome. Incidence of IUGR was significantly higher in scores of 3 (10/11, 91%) than in scores of 0–2 (36/79, 46%, $P < 0.01$, χ^2-test). Among the pregnancies complicated by IUGR, poor perinatal outcome occurred solely in scores of 3 with a statistical significance (4/10 vs 0/36, $P < 0.05$). Figure 2 shows incidence of poor outcome as a function of birthweight percentile. Neonates born to women with scores of 0–2 had good outcomes without respect to birthweight percentile, while neonates with scores of 3 had poor outcomes when their birthweight percentile was less than the third percentile ($P < 0.05$).

Indications for delivery of the 79 women with scores of 0–2 were labor onset ($n = 38$; 48%), term ($n = 19$; 24%), premature rupture of the membranes ($n = 11$; 14%), IUGR ($n = 6$; 8%), pregnancy-induced hypertension ($n = 4$; 5%) and thrombocytopenia ($n = 1$; 1%).

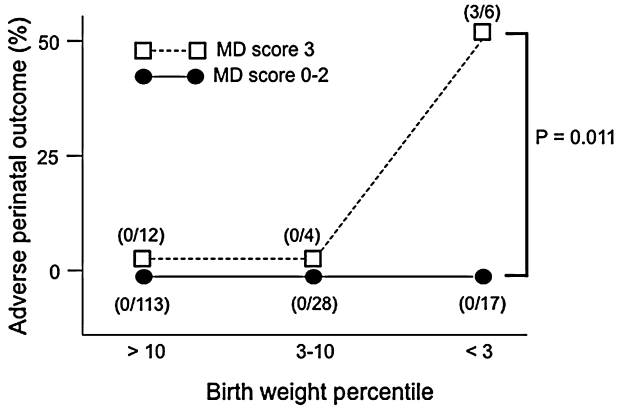

Figure 2 Additive effect of MD-twin score 3 and severe IUGR (<3rd percentile) on the incidence of adverse perinatal outcome. Closed circles represent women with MD-twin scores of 0–2, and open rectangles represent women with MD-twin scores of 3. MD, monochorionic diamniotic; IUGR, intrauterine growth restriction; TTTS, twin-to-twin transfusion syndrome.

Three women scored 3 between 22 and 25 weeks of gestation and were excluded from our primary analyses (Fig. 1). One woman scored 3 at 25 weeks of gestation, improved to a score of 2 between 26 and 28 weeks, but relapsed to a score of 3 at 29 weeks and delivered by cesarean section. Both infants were healthy. Another woman scored 3 at 24 weeks, and remained there until 27 weeks, when one twin showed recurrent late decelerations. We performed emergency cesarean section and both infants had good outcomes. The last woman scored 3 at 24 weeks, and remained there until 28 weeks, when one twin died *in utero* and the other showed tachycardia and was delivered by cesarean section, resulting in neonatal death.

Discussion

We performed a prospective study to see if application of MD-twin score to antepartum management would improve the prognosis of those MD twins who did not meet the criteria of TTTS before 26 weeks of gestation. These women constituted 90% of MD-twin pregnancies. During the study period, a consistent antepartum evaluation method (MD-twin score) and appropriate perinatal support was provided in a single tertiary center. In this clinical situation, applying MD-twin score results in a significant reduction in the incidence of poor outcomes (death or neurological damage), from 22% (13/59) to 4% (4/90), when we compared the present study's results with our previous study.[9] Briefly, in the previous study we retrospectively investigated 59 MD twins who were delivered after 26 weeks of gestation. Some fetal tests were used to determine delivery timing, such as fetal heart rate monitoring and biophysical profile scoring (commonly used in the contemporary management of twin pregnancies).

In this study, TTTS occurred in 12% of MD twins before 26 weeks of gestation. This incidence is consistent with previous reports.[16,17] The remaining 90% were non-TTTS and assigned to conservative management such as serial ultrasound examination, fetal heart rate monitoring and biophysical profile scoring.[8,10,18] However, recent studies have shown 2–3% rate of unexplained fetal death after 32 weeks of gestation in MD-twin pregnancies, even though they did not have TTTS or IUGR.[8,10] Furthermore, even in the absence of either TTTS or a single intrauterine fetal death, neuromorbidity is significantly increased in MD twins (1.7%) compared with dichorionic twins (12%).[19] These results suggest that proper fetal surveillance is required for non-TTTS MD twins to decrease morbidity and mortality. For this purpose, we introduced the MD-twin score, and the present prospective study confirmed its clinical usefulness.

Three cases of adverse outcome were associated with severe IUGR (Table 3). They are compatible with selective IUGR, in which fetal weight less than the 10th percentile in one fetus without apparent TTTS is widely accepted.[20] This condition is an important contributor to perinatal mortality and morbidity in MD twins and is associated with higher risk of neurological damage. This study showed that severe IUGR (<3rd percentile) and an MD-twin score of 3 acted additionally to cause poor outcome (Fig. 2). On the other hand, MD twins with scores of 0–2 did not have poor outcomes, even if complicated with selective IUGR. However, we could not determine when MD twins complicated by selective IUGR should be terminated. Recently, Gratacos *et al*. have proposed a classification system of selective IUGR into three types according to umbilical artery Doppler patterns in the fetus with IUGR.[21] Accordingly, pregnancies were defined as type I (normal umbilical artery Doppler), type II (persistently absent or reversed end-diastolic flow) or type III (intermittently absent or reverse end-diastolic flow). They showed that the umbilical artery Doppler pattern observed at the time of the diagnosis of selective IUGR correlated with distinct clinical behavior and placental features. Further studies are required to determine how selective IUGR could be combined with the MD-twin scoring system to further improve perinatal outcomes.

Four MD twins with poor outcomes had fetal weight discordance. The inter-twin fetal weight discordance in absence of TTTS, or isolated discordant growth, is defined as an inter-twin size difference of 25% or more.[17] Isolated discordant growth is another factor that increases mortality and morbidity of MD twins. Approximately 20% of pairs with discordant growth progress to TTTS.[17] Even without TTTS, isolated discordant growth diagnosed in the second trimester results in a 25% fetal death rate, most often affecting the smaller twin.[22–24] While the pathogenesis of isolated discordant growth is currently poorly understood, various placental anatomical features have been implicated.[25] In this study, peripheral cord insertion was documented in these three cases.

The definition of amniotic fluid discordance employed in this study is different from that of Quintero's criteria. Amniotic fluid discordance is observed not only for TTTS but also for isolated discordant growth. The smaller twin will usually produce less urine than its larger co-twin due to its smaller size. Moreover, in a manner similar to growth-restricted singletons, the smaller twin may develop oligohydramnios. It appears that amniotic fluid discordance represents a heterogeneous group having various types of underlying placental pathophysiology. The amniotic fluid discordance may reflect a moderate imbalance in net blood flow via placental anastomoses, which may be combined with unequal placental sharing and lead to selective IUGR. We determined amniotic fluid discordance to be oligohydramnios (2 cm maximum vertical pocket) in one, and hydramnios (≥8 cm) in the other. In our study, amniotic fluid discordance was caused by oligohydramnios of the growth-restricted

twin and resulted in a poor outcome. Huber *et al*. showed a similar finding, that MD pregnancies presenting amniotic fluid discordance represent a high-risk group for adverse pregnancy outcome, particularly if IUGR and absent or reversed end-diastolic umbilical artery flow are present in the smaller twin.[26] Further study is needed to determine the optimal timing of delivery in cases with amniotic fluid discordance.

This study has several strengths. Management of MD twins has focused on TTTS. Our study concentrated on non-TTTS, constituting 80% of MD twins in the current study, and found that MD-twin score has the potential to improve perinatal outcome. Another point is that this study was performed in the tertiary center where perinatal mortality and morbidity were the lowest in Japan during the study period.

This study also has several limitations. One is that it is not a randomized controlled trial but a prospective single-arm study. Another is that approximately 3% of non-TTTS MD twins were excluded from using the MD-twin score, because these women had a score of 3 before 26 weeks of gestation. This situation presents a dilemma, balancing iatrogenic premature delivery of borderline viability and intrauterine fetal demise and adverse neurological sequelae. Several studies have shown the usefulness of Doppler assessment for unique conditions of MD twins, such as selective IUGR.[19] As MD-twin score did not include Doppler assessment, we were not able to evaluate the association between MD-twin score and Doppler assessment. Still another limitation is related to neonatal cardiovascular impairment. As shown in Table 3, one infant progressed to hypovolemic shock caused by excessive urinary output during the early neonatal course. Because the MD-twin score was originally established to decrease death and neurological damage, it could not directly predict cardiovascular impairment after birth. Neonatal care specialists familiar with cardiovascular changes in MD twins are required.

In conclusion, it is useful to apply the MD-twin score antenatal surveillance of the 90% of MD twin pregnancies that do not have TTTS. An MD-twin score of 2 is reassuring for a good outcome; however, a score of 3 is indicative of a 4% risk of poor outcome.

Acknowledgments

This work was partly supported by a grant (no. 79-258) from the Japan Ministry of Education, Culture, Sports, Science and Technology, and a grant from the Ogyaa-Donation Foundation. We are grateful to Mr Richard White for his assistance in English editing.

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