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# Inter-twin membrane folding in monochorionic pregnancies

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## ABSTRACT

*This study examines the value of assessing inter-twin membrane folding in monochorionic twin pregnancies in the prediction of twin-to-twin transfusion syndrome. In 83 monochorionic twin pregnancies ultrasound scans were carried out at 10–14, 15–17 and 19–21 weeks to investigate folding of the inter-twin membrane as an early sonographic feature of inter-twin discrepancy in amniotic fluid volume. There were 23 (28%) cases of membrane folding, which was first observed in one case at 10–14 weeks, in 21 cases at 15–17 weeks and in another case at 24 weeks. In 12 (52%) of the 23 cases the pregnancy progressed to severe twin-to-twin transfusion syndrome and 10 of these were treated by endoscopic laser coagulation of the placental vascular anastomoses. In the other 11 cases there was a moderate syndrome with large discrepancies in amniotic fluid volume and fetal size, persisting throughout pregnancy. In the severe group, five pregnancies resulted in live birth of both babies, three in live birth of one and intrauterine death of the other twin and in four cases there were no survivors. In the moderate group, all babies survived and the inter-twin disparity in birth weight was more than 20%. Similarly, all 60 pregnancies with no membrane folding resulted in live births. In all three groups there was an increase in inter-twin disparity in fetal size with gestation and the greatest inter-twin disparities were in those with moderate twin-to-twin transfusion syndrome from as early as the 10–14-week scan. These findings demonstrate that folding of the inter-twin membrane occurs in about one-quarter of monochorionic twins and in about half of these there is subsequent development of severe twin-to-twin transfusion syndrome.*

## INTRODUCTION

Communicating vascular anastamoses are present in all monochorionic placentas[1], but severe twin-to-twin transfusion syndrome supervenes in only about 10–15% of cases[2]. Severe twin-to-twin transfusion syndrome characteristically presents at 16–24 weeks of gestation with the anhydramnios/polyhydramnios sequence[3]. We have recently observed that an early feature of the developing syndrome is a discrepancy in amniotic fluid volume, manifested as folding of the inter-twin membrane (Figure 1).

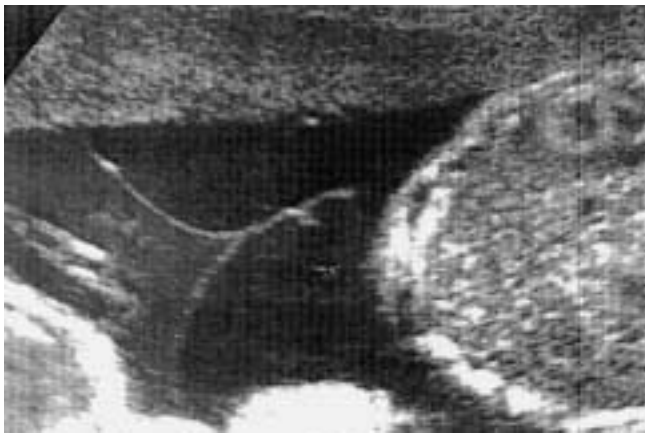

**Figure 1** Ultrasound image of a monochorionic twin pregnancy at 15–17 weeks of gestation, demonstrating folding of the inter-twin membrane and discrepancy in echogenicity of amniotic fluid characteristic of discordancy in amniotic fluid volume with developing twin-to-twin transfusion syndrome

The aim of this study was to examine the prevalence and significance of this ultrasonographic feature in monochorionic twins.

## METHODS

This was a prospective ultrasonographic study of 83 monochorionic–diamniotic twin pregnancies identified at 10–14 weeks of gestation, when the women attended our center for assessment of risk for trisomy 21 by a combination of maternal age and fetal nuchal translucency thickness[4,5]. Demographic details and ultrasound findings were entered into a computer database at the time of scanning. Twin pregnancies were classified as dichorionic or monochorionic according to the presence or absence of an extension of placental tissue into the base of the inter-twin membrane, visualized by ultrasonography as the lambda sign and T sign, respectively[6,7]. Patients with monochorionic pregnancies were requested to attend for further ultrasound examinations at 15–17 weeks and 19–21 weeks

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for early diagnosis of possible twin-to-twin transfusion syndrome.

The diagnosis of severe twin-to-twin transfusion syndrome was based on the demonstration of anhydramnios and non-visible bladder in the presumed donor fetus, in combination with polyhydramnios and a dilated bladder in the recipient fetus. A moderate syndrome was diagnosed if, in addition to a subjective major discrepancy in the amniotic fluid volume of the two sacs, there was folding in the inter-twin membrane (Figure 1). Patients with severe twin-to-twin transfusion syndrome were counselled as to the available options of expectant management, amniodrainage or endoscopic laser coagulation of the communicating placental vessels. In those with moderate twin-to-twin transfusion syndrome, ultrasound examinations were carried out at weekly intervals until resolution of the disparity in amniotic fluid volumes or the development of a severe condition.

The significance of comparisons of inter-twin disparity in fetal size (expressed as a percentage of the larger twin) between the groups was assessed by the Mann–Whitney *U* test and the significance of trend in inter-twin disparity in fetal size with gestation was examined with Cuzick's test for trend.

## RESULTS

In the 83 cases, 12 developed features of severe twin-to-twin transfusion syndrome and 11 developed moderate twin-to-twin transfusion syndrome (Table 1). At the 10–14-week scan, folding of the inter-twin membrane was observed in one of the 83 pregnancies; in this case there was progression to a severe condition treated by endoscopic laser at 15 weeks. At the 15–17-week scan, a moderate condition was observed in 21 of the remaining 82 pregnancies. In 11 of these there was subsequent development of severe twin-to-twin transfusion syndrome; in nine, endoscopic laser coagulation was carried out at 16–24 weeks. In one, there was intrauterine death of both fetuses at 18 weeks, and in another there was an intrauterine death of the donor with survival of the recipient at 23 weeks, before planned endoscopic laser coagulation was carried out. In the other 10 cases there was persistence of the features of moderate twin-to-twin transfusion syndrome throughout pregnancy. At the 19–21-week scan, there was no evidence of disparity in amniotic fluid in any of the 61 cases that did not have features of twin-to-twin transfusion syndrome in their previous scans. However, one of these patients developed polyhydramnios at 24 weeks with membrane folding and was treated by amniodrainage at 28 and 29 weeks.

In the 60 cases with no antenatal features of twin-to-twin transfusion syndrome, all babies were live born at 31–40 (median 37) weeks of gestation. Similarly, in the 11 cases with moderate twin-to-twin transfusion syndrome, all babies were live born at 27–37 (median 34) weeks of gestation, but one baby died in the neonatal period owing to prematurity. In the severe group, five pregnancies resulted in live birth of both babies, three in live birth of one and intrauterine death of the other and in four cases there were no survivors.

In the normal, moderate and severe pregnancies there was an increase in inter-twin disparity in fetal size with gestation ($z = 3.4$, $p < 0.001$; $z = 4.0$, $p < 0.001$; $z = 2.7$, $p = 0.01$, respectively; Table 2). The highest inter-twin disparities in size were observed in the moderate group and

**Table 1** Gestation at which folding of the inter-twin membrane was observed, management and outcome in 23 monochorionic pregnancies with twin-to-twin transfusion syndrome (TTS)

| *Case* | *Gestation at membrane folding* (weeks) | *Type of TTS* | *Gestation at which observed* (weeks) | *Treatment* | *Outcome* |
|---|---|---|---|---|---|
| 1 | 13 | severe | 15 | laser | IUD 15 weeks / LB 31 weeks |
| 2 | 15 | severe | 16 | laser | IUD 16 weeks / LB 38 weeks |
| 3 | 16 | severe | 21 | laser | LB / LB 33 weeks |
| 4 | 16 | severe | 20 | laser | LB / LB 31 weeks |
| 5 | 16 | severe | 18 | none | IUD / IUD 18 weeks |
| 6 | 16 | severe | 23 | none | IUD 23 weeks / LB 35 weeks |
| 7 | 16 | severe | 20 | laser | LB / LB 32 weeks |
| 8 | 16 | severe | 21 | laser | LB / LB 34 weeks |
| 9 | 16 | severe | 17 | laser | IUD / IUD 18 weeks |
| 10 | 17 | severe | 24 | laser | NND / NND 24 weeks |
| 11 | 17 | severe | 19 | laser | LB / LB 38 weeks |
| 12 | 17 | severe | 20 | laser | IUD 20 weeks / IUD 21 weeks |
| 13 | 15 | moderate | | expectant | LB / LB 35 weeks |
| 14 | 15 | moderate | | expectant | LB / LB 37 weeks |
| 15 | 16 | moderate | | expectant | LB / LB 37 weeks |
| 16 | 16 | moderate | | expectant | LB / NND 27 weeks |
| 17 | 16 | moderate | | expectant | LB / LB 35 weeks |
| 18 | 16 | moderate | | expectant | LB / LB 32 weeks |
| 19 | 16 | moderate | | expectant | LB / LB 29 weeks |
| 20 | 16 | moderate | | expectant | LB / LB 32 weeks |
| 21 | 16 | moderate | | expectant | LB / LB 36 weeks |
| 22 | 17 | moderate | | expectant | LB / LB 34 weeks |
| 23 | 24 | moderate | | amniodrainage | LB / LB 32 weeks |

IUD, intrauterine death; NND, neonatal death; LB, live birth

**Table 2** Inter-twin disparity in fetal size, expressed as a percentage of the value of the larger twin, in monochorionic twin pregnancies with or without twin-to-twin transfusion syndrome (TTS). Values shown are medians, with ranges in parentheses. At 10–14 weeks, fetal crown–rump length (CRL) was used as an indicator of fetal size, whereas, at 15–17 weeks and 19–21 weeks, estimated fetal weight (EFW) was used, calculated from the formula of Hadlock and colleagues[17]

| | *Inter-twin disparity* (%) | | | |
|---|---|---|---|---|
| | *No TTS* | *Moderate TTS* | *Severe TTS* | *Statistics* |
| CRL at 10–14 weeks | 4.5 (0–16.3) | 13.0 (0–24.2) | 5.2 (0–14.5) | no TTS vs. moderate: $t = 2.9$, $p = 0.004$<br>no TTS vs. severe: $t = 0.2$, $p = 0.81$<br>moderate vs. severe: $t = 2.1$, $p = 0.04$ |
| EFW at 15–17 weeks | 5.1 (0–17.9) | 22.3 (6.9–39.4) | 13.2 (1.1–28.2) | no TTS vs. moderate: $t = 4.6$, $p < 0.001$<br>no TTS vs. severe: $t = 2.7$, $p = 0.01$<br>moderate vs. severe: $t = 2.1$, $p = 0.03$ |
| EFW at 19–21 weeks | 7.0 (1.0–28.3) | 24.1 (11.3–50.9) | — | no TTS vs. moderate: $t = 4.6$, $p < 0.001$ |
| Birth weight | 7.1 (0.8–29.9) | 28.1 (20.6–64.9) | — | no TTS vs. moderate: $t = 4.8$, $p < 0.001$ |

this disparity was significantly higher than in the group without and in that with severe twin-to-twin transfusion syndrome from as early as the 10–14-week scan (Table 2; Figure 2). The inter-twin disparity in birth weight was more than 20% in all cases with moderate twin-to-twin transfusion syndrome and in 10% of the group without the condition. For the severe group, the number of cases with two live fetuses and no intervention was too small beyond the 15–17-week scan for valid comparisons to be made with the other groups.

## DISCUSSION

This study has demonstrated that, in about a quarter of monochorionic twin pregnancies at 15–17 weeks of gestation, there was a fold in the inter-twin membrane which is an early manifestation of disparity in amniotic fluid volume due to twin-to-twin transfusion syndrome. In about half of such cases with membrane folding there was progression to the polyhydramnios/anhydramnios sequence and in the other half there was moderate twin-to-twin transfusion syndrome. The inter-twin disparity in size was more marked at all gestations in the moderate compared to the severe groups.

In a screening study involving 485 twin pregnancies with live fetuses at the 10–14-week scan, the risks for subsequent miscarriage before 24 weeks of gestation and perinatal death after 24 weeks were 2% and 1%, respectively, for dichorionic twins and 12% and 2%, respectively, for monochorionic twins[8]. It was postulated that the high risk for fetal loss in monochorionic twins could be attributed to the development of twin-to-twin transfusion syndrome. This is confirmed by the findings of the present study which has in addition demonstrated that folding of the inter-twin membrane at 15–17 weeks constitutes an early sonographic marker for twin-to-twin transfusion syndrome. Furthermore, in about 75% of monochorionic twins there was no membrane fold and these pregnancies are not at increased risk for miscarriage or perinatal death.

In the pediatric literature, the diagnosis of twin-to-twin transfusion syndrome has traditionally been based on the demonstration of large (more than 20%) inter-twin disparity in birth weight[9,10]. These observations are compatible with our findings in the moderate group that was managed expectantly and resulted in live births with large inter-twin disparities in birth weight. In severe twin-to-twin transfusion syndrome presenting with acute tense polyhydramnios at 16–24 weeks of gestation, survival with expectant management is less than 10%[11]. Improved survival in such pregnancies has been reported after treatment with serial amniocenteses and drainage of large volumes of amniotic fluid; this treatment presumably prevents the polyhydramnios-mediated risk of spontaneous abortion or very premature delivery. In studies published before 1991 amniodrainage was associated with survival in 30–40% of cases[11]. However, five recent papers from three centers have reported survival of 72–83% of fetuses and the proportion of pregnancies with at least one survivor was 81–100%[12–16]. It is possible that the apparent marked improvement in survival with serial amniodrainage, compared to previous studies that used the same treatment protocols, could, at least in part, be the consequence of the inclusion of pregnancies with moderate twin-to-twin transfusion syndrome. Thus, the widespread use of routine ultrasound examination and the identification of monochorionic pregnancies with large inter-twin disparities in size and amniotic fluid volume (our moderate twin-to-twin transfusion syndrome group), could have stimulated obstetricians to undertake amniodrainage in pregnancies that, according to the findings of the present study, would have resulted in live births even without such treatment. Since in only about 50% of pregnancies with twin-to-twin transfusion syndrome is the condition severe (where amniodrainage may truly be associated with a survival of 40%), the inclusion of pregnancies with the moderate condition (where survival even with expectant management may be as high as 100%) could account for the apparent recent improvement in survival with amniodrainage from about 40% to 70%.

This study has highlighted the presence of two types of twin-to-twin transfusion syndrome presenting with large inter-twin disparities in size and amniotic fluid volume. In the first group, which we classified as severe, the predominant disparity was in amniotic fluid volume with anhydramnios in the presumed donor fetus and polyhydramnios in the recipient twin. In the second group, classified as moderate, the predominant disparity was in fetal size which was apparent from at least as early as

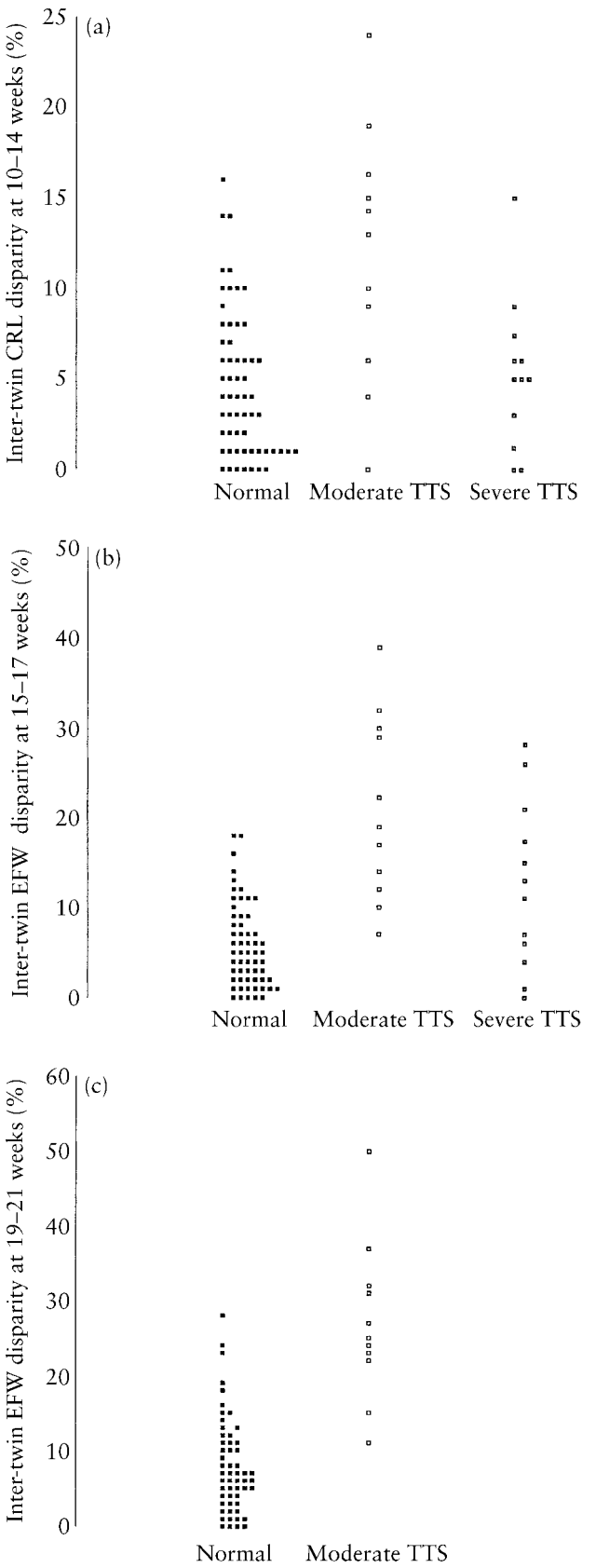


**Figure 2** Inter-twin disparity in fetal size, expressed as a percentage of the larger twin, in 83 monochorionic pregnancies without twin-to-twin transfusion syndrome (TTS) (normal), and with moderate or severe TTS at 10–14 weeks (a), 15–17 weeks (b) and 19–21 weeks of gestation (c). CRL, crown–rump length; EFW, estimated fetal weight

10–14 weeks of gestation. The extent to which these apparently distinct clinical presentations are the consequence of such factors as the timing and degree of unequal splitting of the embryonic cell mass, and/or the size, number and type of communicating placental vessels between the two feto-placental circulations, remains to be determined.

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