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Chapter 5

Iatrogenic perforation of the intertwin membranes after laser surgery for twin-twin transfusion syndrome

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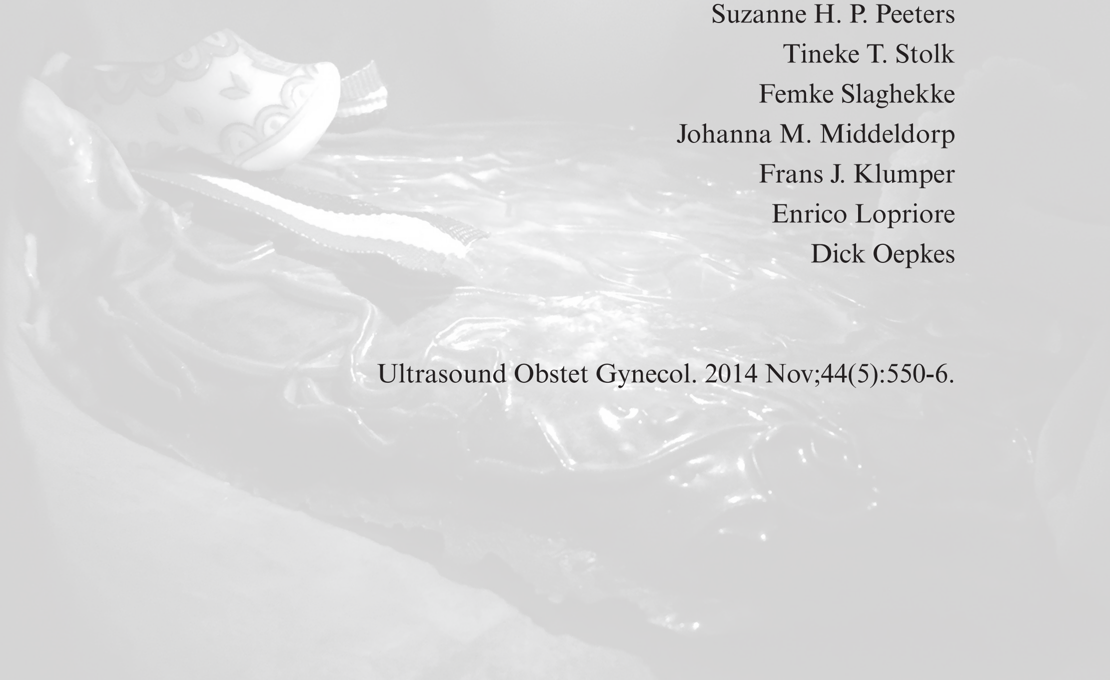

ABSTRACT

Objective To evaluate management and outcome of iatrogenic monoamniotic twins (iMAT) compared with twins with intact intertwin dividing membranes after laser surgery for twin-to-twin transfusion syndrome (TTTS).

Methods This was a retrospective analysis of twins with and without iatrogenic rupture of the intertwin membranes that had been treated for TTTS with laser surgery at our center between 2004 and 2012. Primary outcomes were perinatal survival and severe neonatal morbidity. Secondary outcomes were mode of delivery, gestational age at birth and cord entanglement.

Results In total, 338 pregnancies were included. In 67/338 (20%) pregnancies, iMAT was suspected antenatally. In 47 of these 67 (70%), a preterm Cesarean section was performed for monoamnionicity. Perinatal survival was 108/134 (81%) vs 396/542 (73%) in twins with intact intertwin membranes ($P=0.13$). Mean gestational age at birth in iMAT was 31 completed weeks, compared to 33 weeks in twins with intact membranes ($P<0.01$). At birth, cord entanglement was present in 8/67 (12%) iMAT pregnancies. Severe neonatal morbidity was assessed in 106/110 (96%) in iMAT cases and 392/416 (94%) in controls. The incidence of severe neonatal morbidity was 28/106 (26%) in iMAT vs 72/392 (18%) in controls ($P=0.25$). Severe cerebral injury was significantly increased in the iMAT group as compared with controls, at 16/106 (15%) vs 18/392 (5%) ($P<0.01$).

Conclusions Iatrogenic rupture of intertwin membranes was suspected in 20% of pregnancies treated with laser therapy for TTTS and was associated with a lower gestational age at birth and increased neonatal morbidity.

INTRODUCTION

Twin-to-twin transfusion syndrome (TTTS) is a serious complication of monochorionic twin gestations, with a high risk of perinatal morbidity and mortality. Fetoscopic laser photocoagulation of the vascular anastomoses is the preferred treatment, with an overall survival of up to 74%.[1] As it is an invasive procedure, perioperative complications of laser surgery itself increase the risk of adverse outcome.[2] One of these complications is unintentional perforation of the intertwin dividing membranes, thereby creating an iatrogenic monoamniotic twin (iMAT) pregnancy.

Rupture of intertwin membranes can occur as a consequence of perforation of the donor's collapsed membrane at the trocar insertion site, which may be invisible on ultrasound. Another mechanism for perforating the membranes is by coagulation of vascular anastomoses through the membrane, which is sometimes unavoidable. iMAT is reported to occur in 1.3–8.7% of cases and is associated with preterm prelabor rupture of membranes (PPROM), premature delivery, pseudo-amniotic band syndrome and complications due to cord entanglement, as seen in spontaneous monoamniotic twins.[2–4] There have been only a few reports on iMAT as a complication of invasive procedures.[2–4] Clinical implications of iMAT and optimal management strategies in these pregnancies have not been established. Since perforation is not always detected during or directly after surgery, this diagnosis can be easily missed, unless specific attention is given to its features during follow-up examinations.

If iMAT is suspected, pregnancies are often more closely monitored, hospitalization after viability is considered and a preterm, elective Cesarean section is scheduled between 32 and 34 weeks' gestation to prevent cord accidents. Uncomplicated monochorionic twin pregnancies after laser surgery are often allowed to continue to around 36 weeks. We therefore hypothesized that iMAT could be associated with a lower gestational age at birth as compared with twins with intact intertwin membranes after laser treatment, with concomitant adverse effects on neonatal morbidity.[5]

The aim of this study was to investigate the incidence of iMAT after laser surgery for TTTS and compare management and perinatal outcomes of suspected iMAT cases with those of twins with intact intertwin membranes.

METHODS

At Leiden University Medical Center, the Dutch national tertiary referral center for invasive fetal therapy, fetoscopic laser surgery has been the preferred treatment modality for all pregnancies complicated by TTTS Quintero stage II or higher, and for selected cases with Quintero stage I with symptomatic polyhydramnios, since August 2000. Chorionicity and amnionicity are established by sonographic examination in the first trimester of pregnancy. The diagnostic (established) criteria for TTTS are defined according to the Eurofoetus protocols.[6]

In this study fetoscopic surgery was performed by one of four specialized surgeons after written consent of the patient had been obtained. All procedures were performed through a single percutaneous port in the recipient sac, except for a few cases with completely anterior placenta, in which introduction of the shaft in the posterior uterine wall was assisted by open-entry laparoscopy under general anesthesia, a technique that was used until 2009.[7]

Fetoscopic procedures were performed using a 1.3-mm or 2.0-mm semi-rigid or rigid fetoscope or a 1.0-mm embryoscope (Storz, Vianen, The Netherlands), introduced through operative fetoscopic sheaths and trocars with maximum external diameters of 8 or 10 French, depending on placental location and gestational age. If necessary, Ringer's lactate warmed to body temperature was infused to improve distention or visualization. Coagulation of the anastomoses was performed using a diode laser (Diomed Limited, Cambridge, UK) or Nd:YAG laser (Dornier Medizin Technik, Germering, Germany). The technique used for the laser procedure was adapted over the years; selective sequential laser was performed from 2006. The 'Solomon technique' (coagulation of the complete vascular equator after selective sequential laser) was introduced in March 2008. A subset of the patients (n=141) included in this study also participated in the Solomon trial.[1] At the end of the procedure, amniotic fluid was drained until the deepest amniotic fluid pocket was<6 cm on ultrasound examination.

Complications and technical difficulties such as (un)intentional perforation of the intertwin membranes, significant intra-amniotic bleeding or incomplete procedure were documented directly after surgery. Ultrasound examination was performed within 24 h after surgery to detect early iMAT and then at least biweekly at our center by highly specialized sonographers or by shared care with referring centers. A standardized ultrasound follow-up protocol was used from 2004 for all patients treated with laser therapy, including specific assessment of the intertwin membranes as a standard element of care.

Perforation of the intertwin membranes was diagnosed either by direct observation of a gradual filling of the donor sac at the time of the fetoscopic procedure or during the follow-up ultrasound examination (on the first postoperative day, or later) if increased amniotic fluid was noted in the donor sac in conjunction with free-floating intertwin membrane and a non-cycling donor bladder and/or entanglement of the cords was suspected.[8]

After delivery, the presence of cord entanglement was noted, and macroscopic examination of the placenta and membranes was performed to confirm the diagnosis of monoamnionicity.

For this study we performed a retrospective analysis of prospectively collected data on perinatal outcome and management of all pregnancies with TTTS treated at our center. Data on obstetric and neonatal outcomes were derived from medical charts. In cases in which the delivery did not take place at our center, data were provided by outcome reports from the referring obstetricians and pediatricians.

Since iatrogenic rupture of the membranes was underreported in the first years after the start of laser therapy, we included only cases from 2004 (after we started using a standardized follow-up protocol) until 2012, to exclude reporting bias. We included all monochorionic twin pregnancies complicated by TTTS treated with fetoscopic laser coagulation, not clinically in labor at the time of the procedure. Triplet pregnancies, twins with one or more major congenital anomalies or chromosomal abnormalities, sonographic evidence of perforation of intertwin membranes prior to laser therapy and spontaneous monoamniotic pregnancies were excluded from this study. None of the pregnancies was excluded from analysis once the fetoscope had been introduced into the amniotic cavity, even if laser coagulation was not possible.

Primary outcomes were perinatal survival at 4 weeks of age and severe neonatal morbidity. Secondary outcomes included PPROM, gestational age at birth, birth weight and the need to perform a re-intervention. Severe neonatal morbidity was defined as the presence of at least one of the following: respiratory distress syndrome (requiring medical ventilation and surfactant), patent ductus arteriosus (requiring medical therapy or surgical closure), right ventricular outflow tract obstruction, renal failure, necrotizing enterocolitis ≥Grade 2, amniotic band syndrome, ischemic limb injury or severe cerebral injury. Severe cerebral injury included at least one of the following: intraventricular hemorrhage ≥Grade III, cystic periventricular leukomalacia ≥Grade II, ventricular dilatation above 2 SDs (including posthemorrhagic ventricular dilatation), intraparenchymal echodensities, porencephalic or parenchymal cysts, arterial infarction, congenital brain malformation or other severe cerebral lesions associated with adverse neurological outcome.[9]

Statistical analysis

Patients were categorized into one of two groups: pregnancies in which perforation of the intertwin membranes was antenatally suspected (iMAT) and pregnancies with intact intertwin membranes. Intentional perforation of the intertwin membranes was applied only in a few exceptional cases, however all cases with intentional or unintentional membrane perforation were included in the analysis. Continuous variables were reported as median (range) or mean (SD); group differences were compared using the Mann–Whitney *U*-test or independent Student's *t*-test. Proportions were compared using the chi-square test or Fisher's exact test, as appropriate. All analyses per fetus or neonate were performed using the generalized estimated equation module to account for the effect that observations between cotwins are not independent. Statistical analysis was performed with SPSS version 21.0 (SPSS IBM, New York, NY, USA), and $P<0.05$ was considered to be statistically significant.

RESULTS

Laser coagulation was performed in 338 pregnancies fulfilling the inclusion criteria. iMAT was suspected antenatally in 67/338 (20%) cases; in 39/67 (58%), this was within 24 h after surgery. No significant differences in perioperative variables (i.e. maternal age, severity of TTTS, location of placenta, introduction technique, laser technique or fetoscopy time) were detected, except for mean gestational age at surgery, which was 21 weeks in iMAT and 20 weeks in cases with intact membranes ($P<0.01$). Detection of iMAT was not associated with laser surgery performed after 26 weeks' gestation; 4/67 (6%) *vs* 14/271 (5%) ($P=0.76$). Visibility was reduced by significant intra-amniotic bleeding in 9% of procedures, a similar percentage in both groups.

Characteristic	iMAT (n=67)	Intact membranes (n= 271)	P value
Maternal age (years, mean (range))	30 (20–41)	31 (19–42)	0.28
Placental location			0.24
Anterior	34 (51)	116 (43)	
Posterior	33 (49)	155 (57)	
Quintero stage			0.32
I	3 (4)	25 (9)	
II	17 (25)	88 (32)	
III	44 (66)	146 (54)	
IV	3 (4)	12 (4)	
Introduction technique			0.16
Percutaneous	59 (88)	254 (94)	
Mini-laparotomy	—	2 (1)	
Combined open laparotomy for anterior placenta	8 (12)	15 (6)	
Laser technique			0.31
Selective	53 (79)	198 (73)	
Solomon	14 (21)	73 (27)	
GA at laser (weeks, mean (range))	21 + 0 (15 + 3 to 29 + 5)	19 + 6 (13 + 3 to 29 + 1)	< 0.01
Laparoscopy time (min, median (range))	30 (5–100)	29 (8–113)	0.29
Significant intra-amniotic bleeding during procedure	6 (9)	20 (7)	0.73
Re-intervention necessary	12 (18)	19 (7)	< 0.01
Indication for re-intervention			0.79
Recurrence/reversal	8/12 (67)	10/19 (53)	
TAPS	2/12 (17)	5/19 (26)	
Severe cerebral injury	1/12 (8)	1/19 (5)	
Other	1/12 (8)	3/19 (16)	
Type of re-intervention			0.78
Laser	3/12 (25)	3/19 (16)	
Amniodrainage	2/12 (17)	4/19 (21)	
IUT	3/12 (25)	5/19 (26)	
Selective feticide	3/12 (25)	7/19 (37)	
Laser + IUT	1/12 (8)	—	

Data given as *n* (%) unless indicated.

GA, gestational age; TAPS, twin anemia–polycythemia sequence; IUT, intrauterine transfusion.

Table 1 Baseline characteristics of 338 pregnancies treated for twin-to-twin transfusion syndrome, according to whether laser surgery perforated the intertwin membrane (iatrogenic monoamniotic twin (iMAT)) or not

Overall perinatal survival rate in this cohort was 504/676 (75%), with a mean gestational age at birth of 31+6 (range, 24+0 to 41+2) weeks. Perinatal survival at 4 weeks was not significantly different between the groups: 108/134 (81%) in iMAT cases *vs* 396/542 (73%) in cases with intact membranes (P=0.13). Fetal demise occurred in 24/134 (18%) in the iMAT group and 126/542 (23%) in the group with intact membranes (P=0.27). In the iMAT group, there was one case of double fetal demise, which occurred at 25 weeks' gestation, in which cord entanglement was the most likely cause of death. In the control group none of the cases of fetal demise was related to cord entanglement. Neonatal death was observed in 2/110 (2%) and 20/416 (5%) in the iMAT group and the intact-membranes group, respectively (*P*=0.17). Details of pregnancy outcomes per group are summarized in Table 2.

In the iMAT group, PPROM before 32 weeks' gestation occurred more frequently; 32/67 (48%) *vs* 74/271 (27%), although the difference did not reach statistical significance (*P*=0.15).

Pregnancies complicated by iMAT had a significantly higher rate of preterm birth before 32 weeks of 39/67 (58%), compared with 101/271 (37%) in pregnancies with intact membranes (*P*<0.01). Accordingly, the birth weight of liveborn children was significantly lower in the iMAT group (1524 (range, 607–2765) g) than in the intact-membranes group (1936 (range, 585–4190) g; *P*<0.01). Iatrogenic preterm delivery before 32 weeks in cases of iMAT occurred in 10/67 (15%), compared with 22/67 (33%) cases with spontaneous preterm delivery and seven cases of immature delivery or double fetal demise. Additionally, in 16 cases, iatrogenic preterm delivery was induced between 32 and 35 weeks' gestation because of iMAT.

Twenty-eight of the 526 (5%) liveborn neonates were lost to follow-up and excluded from the analysis of morbidity. Severe neonatal morbidity was assessed in 106/110 (96%) iMAT cases and 392/416 (94%) controls. Severe neonatal morbidity was more frequently observed in the iMAT group than in the twins with intact membranes (28/106 (26%) *vs* 72/392 (18%), respectively), but the difference was not statistically significant (*P*=0.25). Severe cerebral injury was significantly more common in the iMAT group (16/106 (15%) *vs* 18/392 (5%); *P*<0.01), as well as the occurrence of respiratory distress syndrome (RDS) (23/106 (22%) *vs* 43/392 (11%); *P*=0.05) and necrotizing enterocolitis (5/106 (5%) *vs* 1/392 (0.3%); *P*=0.01). Amniotic band syndrome was diagnosed in four cases, all within the group with intact intertwin dividing membranes.

Outcome	iMAT (n=67)	Intact membranes (n= 271)	P value
Perinatal survival (at 28 days)*	108/134 (81)	396/542 (73)	0.13
IUFD*	24/134 (18)	126/542 (23)	0.27
Double IUFD	7/67 (10)	28/271 (10)	
NND*	2/110 (2)	20/416 (5)	0.17
PPROM < 32 weeks	32/67 (48)	74/271 (27)	0.15
Preterm birth < 32 weeks	39/67 (58)	101/271 (37)	< 0.01
Mode of delivery†			< 0.01
Vaginal	20/67 (30)	197/262 (75)	
Cesarean section	47/67 (70)	62/262 (24)	
1st vaginal, 2nd Cesarean section	—	3/262 (1)	
GA at birth (weeks)‡	31 + 0 (26 + 0 to 36 + 5)	33 + 4 (24 + 0 to 41 + 2)	< 0.01
Birth weight (g)*, ‡	1524 (607–2765)	1936 (585–4190)	< 0.01
Severe neonatal morbidity*, §, ¶	28/106 (26)	72/392 (18)	0.25
Severe cerebral injury*, ¶, **	16/106 (15)	18/392 (5)	< 0.01
RDS*	23/106 (22)	43/392 (11)	0.05
PDA*	5/106 (5)	7/392 (2)	0.18
RVOTO*	1/106 (1)	3/392 (1)	0.87
Renal failure*	1/106 (1)	2/392 (1)	0.63
NEC*	5/106 (5)	1/392 (0.3)	0.01
Amniotic band syndrome††	—	4/392 (1)	0.50
Ischemic limb injury††	—	2/392 (1)	0.14
Only comfort care because of severe prematurity††	—	9/392 (2)	0.84

Data given as *n* /*N* (%) or mean (range).

* Measured per fetus using the generalized estimated equation module.

† Mode of delivery was unknown in 9/271 cases in the intact-membranes group.

‡ Live births.

§ Severe neonatal morbidity includes at least one of the following: respiratory distress syndrome (RDS) (requiring medical ventilation and surfactant), patent ductus arteriosus (PDA) (requiring medical therapy or surgical closure), right ventricular outflow tract obstruction (RVOTO), renal failure, necrotizing enterocolitis (NEC) ≥ Grade 2, amniotic band syndrome, ischemic limb injury or severe cerebral injury.

¶ Denominator is number of liveborn neonates (excluding those lost to follow-up).

** Severe cerebral injury includes at least one of the following: intraventricular hemorrhage ≥ Grade III, cystic periventricular leukomalacia ≥ Grade II, ventricular dilatation (including posthemorrhagic ventricular dilatation) above 2 SD, intraparenchymal echodensities, porencephalic or parenchymal cysts, arterial infarction, congenital brain malformation or other severe cerebral lesions associated with adverse neurological outcome.

†† Measured using the method of Firth.20 GA, gestational age; IUFD, intrauterine fetal demise; NND, neonatal death within 28 days after birth; PPROM, preterm prelabor rupture of membranes.

Table 2 Outcomes of 338 pregnancies treated for twin-to-twin transfusion syndrome, according to whether laser surgery perforated the intertwin membrane (iatrogenic monoamniotic twin (iMAT)) or not

Details of pregnancies in which iMAT was suspected are summarized in Table 3. In 29/67 (43%) of cases the operator was already aware of perforation during the procedure. In 39/67 (58%) iMAT was observed at the first ultrasound scan within 1 day after the procedure. If iMAT was suspected at a later stage of pregnancy (28/67 (42%)), this occurred after a mean of 28 (range, 5–68) days after the procedure. Fetal monitoring was offered in cases with suspected iMAT in 28/67 (42%), starting at a mean gestational age of 28+2 weeks. Monoamnionicity could be confirmed postnatally in 38/67 (57%) cases with suspected iMAT. Medical charts did not provide information on (mono) amnionicity at birth in 29/67 (43%). After birth, cord entanglement was observed in 8/67 (12%) iMAT cases. In none of the cases without antenatal evidence of iMAT was cord entanglement observed after birth.

Patients delivered by Cesarean section in 47/67 (70%) cases. Eight twins with suspected iMAT and two survivors delivered vaginally, because perforation of the intertwin membranes was not communicated to the referring specialist or very early spontaneous delivery occurred (<30 weeks).

Parameter	Value
Operator aware of perforation during procedure	29/67 (43)
Time from procedure to detection	
< 1 day	39/67 (58)
> 1 day	28/67 (42)
Days if detection > 1 day	28 (5–68)
Fetal monitoring	28/67 (42)
Outpatient clinic > once/week	3/28 (11)
Hospitalization	25/28 (89)
GA at start of fetal monitoring(weeks)	28 + 2 (22 + 0 to 33 + 3)
Mode of delivery	
Elective Cesarean section	39/67 (58)
Emergency Cesarean section	8/67 (12)
Vaginal delivery in case of twosurvivors	8/50 (16)
MA confirmed at birth	38/67 (57)
Cord entanglement	
Confirmed at birth	8/67 (12)
No entanglement	23/67 (34)
Unknown	28/67 (42)
Single IUFD directly after laser not related	8/67 (12)

Data given as *n*/*N* (%) or mean (range). GA, gestational age; IUFD, intrauterine fetal demise; MA, monoamnionicity.

Table 3 Details of pregnancies in which iatrogenic monoamniotic twins (iMAT) were suspected (*n* = 67)

DISCUSSION

In this study, antenatal suspected iMAT was found in 20% of TTTS pregnancies treated with laser therapy. Patients with iMAT were more likely to deliver prematurely than were patients with twins with intact membranes, and this was associated with increased neonatal morbidity.

Fetal surgeons need to be aware of this common and clinically relevant complication, and take the utmost care to prevent it from happening. Once iMAT occurs, close monitoring and adaptation of management are required.

A lower incidence than we observed, 7.2%, was described in a prospective cohort study by Cruz-Martinez *et al.*[4] Habli *et al.*[3] reported a rate of occurrence of iMAT of 1.3% (2/152) in a single-center retrospective study. Chmait *et al.*[2] found an incidence of 8.7% with a significant association with preterm birth<32 weeks. All authors mention the importance of careful routine evaluation of the intertwin membranes at every follow-up ultrasound examination.

Previous studies have indicated that unintentional perforation due to intrauterine interventions, such as amniodrainage, may give a false impression of improvement in TTTS.[10,11] This study supports the idea that septostomy as a primary treatment for TTTS is not to be advised, and should be avoided owing to the subsequent surgical challenges that it creates if an operative laser procedure later becomes necessary.[11–13]

An association of iMAT with the risk of pseudoamniotic band syndrome and PPROM was found in previous studies but could not be confirmed in this one despite the higher reported incidence of iMAT.[4,14] Only four cases of amniotic band syndrome were detected in our cohort but, surprisingly, they were only found in the group with intact intertwin membranes. Free-floating fibrous strings of the membranes could increase the risk of pseudo-amniotic band syndrome, but at present the true etiology of this complication has yet to be established. Although, before starting a procedure, the insertion site is carefully chosen, in some cases perforation of the membrane is unavoidable while entering the amniotic cavity. Even more common is the need to coagulate anastomoses on the other side of the membrane, thereby occasionally creating a defect. In some cases the defect in the membranes seems small at first, but can lead to complete rupture of the intertwin membrane.[4] However, using the laser to coagulate anastomoses through the membranes does not necessarily mean the membranes will be perforated. Amniotic fluid and the absorbing capacities of vessels and blood, together with the wavelength of the laser used, have an influence on absorption of the laser energy and its capacity to effect coagulation.[15] These effects allow the surgeon to coagulate the vessels without damaging the membranes.

Signs of iMAT should be actively sought after laser surgery for TTTS, since awareness of this complication may influence obstetric management. Accurate evaluation of the intertwin membranes, especially after a laser procedure, may be challenging. Chorioamniotic separation, remnants of ruptured membranes, amniotic bands, intrauterine synechia or placental interposition may give the false impression of an 'uncomplicated' diamniotic twin pregnancy.[14] Although when perforation occurs it is likely that it happens during the intervention, in our study this was noticed at the time of the surgery or within 1 day after the procedure in only 58% of cases. Close attention to the intertwin membranes is advised during all follow-up ultrasound examinations in these twins. It is important to realize the pitfalls in the diagnosis of amnionicity.[16]
Re-interventions after laser therapy were performed more frequently in cases of iMAT. We therefore hypothesize that iMAT can serve as an indicator for technically difficult procedures. This was also recently advocated by Chmait *et al.*[2] If perforation occurs during surgery, the leakage of fluid behind the membranes often reduces visibility and makes coagulation of the complete vascular equator in that area challenging. Residual anastomoses after incomplete coagulation are the most common cause of severe complications such as recurrence of TTTS or TAPS, and should be prevented.[17]

We found that pregnancies complicated by iMAT are more likely to deliver prematurely, a finding that is in agreement with those of previous studies.[2,4] In this study, monoamnionicity was confirmed at birth in 58% of cases and cord entanglement could be detected in 12%. Possible explanations for this increased risk are the intensive fetal surveillance and preterm elective Cesarean sections that are carried out in this group in order to prevent cord accidents. Since cord entanglement could be confirmed in 12% of iMAT cases after birth, while observed in almost all true monoamniotic twin pregnancies, the increased risk of adverse perinatal outcome in iMAT pregnancies may not only be related to cord entanglement or monoamnionicity itself. It is likely that other factors such as a technically difficult procedure, need for re-intervention and aggressive perinatal management play a role.
An important difference in severe neonatal morbidity in this study was related to the occurrence of RDS and severe cerebral injury. In iMAT cases 23/106 (22%) neonates suffered from RDS compared with 43/392 (11%) in the control group (P=0.05). The criteria for a diagnosis of RDS in this study were restricted to the most severe form of respiratory failure (requiring mechanical ventilation and surfactant). Severe RDS is associated with an increased risk of chronic lung disease and a concomitant increase in rates of adverse long-term outcomes.[18,19]

A limitation of this study is its retrospective design. Despite extensive follow-up according to antenatal care protocols and prospective data collection with specific attention to perforation of the intertwin membranes during the Solomon trial[1], in this study monoamnionicity was confirmed at birth in 40/67 (60%) and not reported in 27/67 (40%) of cases. Therefore, the percentage of true iatrogenic monoamniotic pregnancies after laser treatment is estimated to be at least 12%, but is likely to be higher. Furthermore, some cases with iMAT might have been missed, thereby the rate of iMAT would even be underestimated. While short-term neonatal morbidity could be assessed in 97% of cases, long-term follow-up was not available for this cohort. These endpoints will be a focus of future investigations.

In conclusion, rupture of the intertwin membranes after invasive antenatal interventions is associated with an increased rate of preterm birth, low birth weight and neonatal morbidity. Prospective studies should focus on prevention, detection and optimal management strategies to reduce these risks.

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