Endoscopic Placental Laser Coagulation in Dichorionic and Monochorionic Triplet Pregnancies

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Abstract

Objective: To report the outcome of monochorionic (MC) and dichorionic (DC) triamniotic (TA) triplet pregnancies treated with endoscopic laser coagulation of the communicating placental vessels for severe feto-fetal transfusion syndrome (FFTS) and selective fetal growth restriction (sFGR). **Methods:** Laser surgery was performed at 18 (15–24) weeks' gestation in 11 MCTA and 33 DCTA pregnancies complicated by FFTS and 14 DCTA pregnancies complicated by sFGR. Data from our study and previous reports were pooled using meta-analytic techniques. **Results:** Survival of at least one baby and survival among all fetuses was 97.0 and 72.7% in DCTA pregnancies with FFTS, 78.6 and 52.4% in DCTA pregnancies with sFGR and 81.8 and 39.4% in MCTA pregnancies with FFTS. In the combined data from our study and previous reports, the pooled survival rates in 132 DCTA pregnancies with FFTS were 94.4 and 76.1%, and in 29 MCTA pregnancies with FFTS, they were 80.6 and 57.5%. **Conclusions:** Survival after laser surgery is higher in DC triplets with FFTS than in those with sFGR and in DC than in MC triplets with FFTS.

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Introduction

Monochorionic (MC) pregnancies are often complicated by severe feto-fetal transfusion syndrome (FFTS) and/or selective fetal growth restriction (sFGR). The established treatment of choice in the management of severe FFTS in MC twin pregnancies is endoscopic laser coagulation of the inter-twin communicating placental vessels [1–3]. In sFGR with abnormal Doppler findings in the umbilical artery of the affected fetus, there is a high risk of perinatal death and handicap for both twins; the management for affected pregnancies presenting at midgestation includes endoscopic laser coagulation of the inter-twin communicating placental vessels or cord occlusion of the FGR twin [4–8]. Few studies in a small number of patients have reported on endoscopic laser coagulation of communicating placental vessels for the management of FFTS in MC or dichorionic (DC) triamniotic (TA) triplet pregnancies complicated by FFTS [9–16].

The objectives of this study are to report our experience with endoscopic laser surgery in the management of severe FFTS or sFGR in MC and DC triplet pregnancies and to compare the results with those of previous studies.

Methods

Study Design and Participants

This was a retrospective study of all cases of MCTA and DCTA triplet pregnancies treated by endoscopic laser coagulation of communicating placental vessels at 15–24 weeks' gestation in our fetal medicine centre between 1996 (4 years after we first introduced endoscopic laser surgery in twins [1]) and June 2015. Umbilical cord occlusion was not a treatment option for sFGR or FFTS in our centre. The cases included 11 MCTA and 33 DCTA pregnancies complicated by FFTS and 14 DCTA pregnancies complicated by sFGR without coexisting FFTS.

Chorionicity and amnionicity were established in the first trimester as previously reported [17]. Gestational age was calculated from the crown-rump length of the biggest fetus [18]. The diagnosis of FFTS was made if there was a marked discordance in amniotic fluid volume between the MC fetuses with a deepest vertical pool of ≤2 cm in at least one sac and of ≥8 cm in the other; the severity of the disease was classified as stage I if the Doppler findings in the umbilical artery and ductus venosus of both fetuses were normal and the bladder of the donor was visible, stage II with normal Doppler findings but no visible bladder, stage III with abnormal Doppler findings in either of the MC fetuses and stage IV with presence of ascites or hydrops in either MC fetus [19].

In the DCTA pregnancies, diagnosis of sFGR was based on the demonstration that, firstly, the abdominal circumference at <22 weeks or estimated fetal weight at ≥22 weeks was below the 5th percentile of the appropriate reference range [20–22] and, secondly, the inter-twin discordance in estimated fetal weight (weight difference divided by the weight of the larger twin) was ≥25%; the estimated fetal weight at <20 weeks was derived by the formula by Warsof et al. [23], and at ≥20 weeks it was derived by the formula of Hadlock et al. [21]. In all of our cases of sFGR, there was Doppler evidence of absent or reversed end-diastolic flow in the umbilical artery of the smaller fetus, and they were therefore classified as type II [24].

Endoscopic laser surgery was carried out transabdominally using a semi-rigid 2.0-mm diameter fetoscope (Karl Storz GmbH, Tuttlingen, Germany), through a 3.3-mm diameter cannula (Cook Medical, Bloomington, Ind., USA), after the administration of prophylactic antibiotics and local anaesthesia. In DC triplet pregnancies with FFTS or sFGR, the fetoscope was introduced into the sac of the larger fetus of the MC pair; a 400-μm diameter Nd:YAG laser fibre (Dornier MedTech, Wessling, Germany) and power output of 40 W was used to coagulate the inter-twin communicating placental vessels as previously described for MC twin pregnancies [7]. In MC triplet pregnancies with FFTS, the fetoscope was introduced into the sac of the recipient fetus, and laser was used to coagulate the vessels between this fetus and each of the other two fetuses; subsequently, the fetoscope was advanced through the inter-twin membrane into the sac of one of the other fetuses to coagulate the vascular connections between them. In cases of polyhydramnios, amnioreduction was undertaken through the cannula over a period of 10–15 min to obtain subjective normalization of the amniotic fluid volume. After a period of rest for 1–3 h, the patients were discharged home. Follow-up and management of the pregnancies was usually undertaken in the referral hospitals.

Maternal demographic characteristics, ultrasound findings and details of intrauterine intervention were recorded in a database. Pregnancy outcomes were collected into the same database when they became available from the referring hospitals, general practitioners or from the patients themselves.

Comparison and Synthesis with Results from Previous Studies

Searches of Medline and Embase (August 2015) were performed to identify all studies in the English language that reported on the use of endoscopic laser surgery for at least two triplet pregnancies. The inclusion criteria were DCTA or MCTA pregnancies complicated by FFTS and/or sFGR, treated by endoscopic laser and providing outcome data. In case of data duplication or overlap, only the largest or most recent study with available data was included.

Statistical Analysis

Data from our study and previous reports were pooled using meta-analytic techniques. Random effects models were used to estimate weighted neonatal survival rates, with 95% confidence interval (CI). Heterogeneity between studies was analysed using both Higgins' I^2 and Cochran's Q test [25, 26].

The statistical software package SPSS 20.0 (IBM SPSS Statistics for Windows, version 20.0, IBM Corp., Armonk, N.Y., USA) and StatsDirect version 2.0 (StatsDirect Statistical Software, UK, 2013) were used for data analysis.

Results

Study Population

During the study period of 1996–2015, we performed endoscopic laser coagulation of communicating placental vessels in 47 DCTA and 11 MCTA triplet pregnancies. The DCTA pregnancies included 14 with sFGR type II and 33 with FFTS; in the latter group, the Quintero stage was I in one, II in two, III in 29 and IV in one. In all MCTA pregnancies, the FFTS was stage III or IV; in 6 cases, there was one donor and one recipient, in 4 cases, there were two donors and one recipient, and in 1 case, there was one donor and two recipients.

DCTA Triplet Pregnancies with FFTS

In the group of 33 DCTA triplet pregnancies with FFTS, endoscopic laser surgery was performed successfully in all cases at a median gestational age of 18 (range 15–23) weeks (table 1). There was survival to discharge from hospital in 72.7% babies, and there was at least one survivor in 97.0% of the pregnancies. The median gestational age at delivery of live births was 29 weeks, and 68.8% were born at <32 weeks.

In 15 pregnancies, all three babies survived after delivery at 8–16 weeks following laser surgery. In 10 pregnancies, two babies survived. In 8 cases, the donor triplet died either in utero or in the neonatal period at 1–14 weeks after laser surgery; the recipient triplet and the separate

one were live born and survived. In 1 case, selective feto-cide of the donor twin was carried out by intracardiac injection of potassium chloride immediately after the laser ablation at 17 weeks' gestation because, at presentation, this fetus was found to have ventriculomegaly and hyperechogenicity of the cerebral cortex; the other two babies were born 13 weeks later and survived. In another case, treated at 20 weeks' gestation, selective fetocide of the separate fetus was carried out because of the diagnosis of cerebellar atrophy after presentation with ruptured membranes at 29 weeks' gestation; the other two babies were live born and survived. In 7 pregnancies, both MC twins died, 6 twins within 2 weeks and one set of twins 4 weeks after laser surgery; in these cases, the separate triplet was live born and survived. In 1 pregnancy, all three babies died; the MC pair died 2 weeks after laser, and this was followed by spontaneous birth at 25 weeks' gestation of the separate triplet that died in the neonatal period.

DCTA Triplet Pregnancies with sFGR

In the group of 14 DCTA triplet pregnancies with sFGR, endoscopic laser surgery was performed successfully in all cases at a median gestational age of 18 (range 16–24) weeks (table 1). There was survival to discharge from hospital in 52.4% babies, and there was at least one survivor in 78.6% of the pregnancies. The median gestational age at delivery of live births was 32 weeks, and 45.5% were born at <32 weeks.

In 1 pregnancy, all three babies survived after delivery at 32 weeks' gestation following laser surgery at 18 weeks. In 9 pregnancies, the FGR triplet died within 2 weeks of laser surgery, but the other two babies were live born 6–20 weeks later and survived. In 1 pregnancy, the MC twins died 1 week after laser surgery at 17 weeks; the separate triplet was live born at 37 weeks and survived. In 3 pregnancies, all three babies died; in the first case, there was miscarriage within 1 week of laser surgery, in the second case, the MC pair died within 2 weeks after laser and this was followed by miscarriage of the separate triplet 3 weeks later, and in the third case, the pregnancy progressed uneventfully after laser surgery at 17 weeks' gestation, but all three fetuses died after prelabor amniorrhexis and chorioamnionitis at 28 weeks.

MCTA Triplet Pregnancies

In the first 4 cases of the series, there was laser coagulation of the communicating vessels between the recipient triplet and the other two fetuses. In the subsequent 7 cases, after completion of the first step as above, the fetoscope was advanced through the inter-twin membrane into the sac of one of the other fetuses to coagulate the vascular connections between them.

Endoscopic laser surgery was performed at a median gestational age of 18 (range 16–23) weeks (table 1). There was survival to discharge from hospital in 39.4% babies, and there was at least one survivor in 81.8% of the pregnancies. The median gestational age at delivery of live births was 32 weeks, and 66.7% were born at <32 weeks.

In 1 pregnancy, all three babies survived after delivery at 30 weeks' gestation following laser surgery at 19 weeks. In 2 pregnancies, the donor triplet died within 2 weeks of laser surgery at 16 and 20 weeks' gestation, respectively, but the other two babies were live born 14 and 8 weeks later and survived. In 6 pregnancies, there was only one survivor; donor and recipient triplets died within 4 weeks after laser surgery. In 2 pregnancies, all three babies died; there was miscarriage within 1 week of laser surgery.

Comparison of Survival between the Triplet Pregnancies

Survival of at least one baby in the DCTA pregnancies with FFTS (97.0%) was not significantly different from that in DCTA pregnancies with sFGR (78.6%; p = 0.790) or MCTA pregnancies with FFTS (81.8%; p = 0.276). Overall survival for all fetuses in the DCTA pregnancies with FFTS (72.7%) was significantly higher than in DCTA pregnancies with sFGR (52.4%; p = 0.003) or MCTA pregnancies with FFTS (33.3%; p < 0.0001).

Table 1. Outcome of our triplet pregnancies treated by endoscopic laser surgery

Outcome measure	DCTA, FFTS (n = 33)	DCTA, sFGR (n = 14)	MCTA, FFTS (n = 11)
GA at laser surgery, weeks	18 (15–23)	18 (16–24)	18 (16–23)
Survival			
Three	15 (45.5)	1 (7.1)	1 (9.1)
Two	10 (30.3)	9 (64.3)	2 (18.2)
One	7 (21.2)	1 (7.1)	6 (54.5)
> one	32 (97.0)	11 (78.6)	9 (81.8)
Overall	72 (72.7)	22 (52.4)	13 (39.4)
GA at delivery of live births, weeks	29 (24–36)	32 (28–36)	32 (28–42)
<32 weeks, n/total n (%)	22/32 (68.8)	5/11 (45.5)	6/9 (66.7)

Values are medians (ranges) or n (%), unless otherwise specified. GA = Gestational age.

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Table 2. Studies reporting on endoscopic laser surgery for FFTS in DCTA triplet pregnancies

Study	Period	Median GA at laser surgery (range), weeks	Total, n	Stage 3/4, n (%)	Survival of >1 baby, n/total n (%, 95% CI)	Overall survival, n/total n (%, 95% CI)	Live birth at <32 weeks, n/total n (%, 95% CI)
Van Schoubroeck et al. [9], 2004	1996–2002	20 (18–23)	5	5 (100)	5/5 (100, 47.8–100)	12/15 (80.0, 51.9–95.7)	4/5 (80.0, 28.4–99.5)
De Lia et al. [11], 2009	1992–2008	21 (18–25)	8	7 (87.5)	8/8 (100, 63.1–100)	20/24 (83.3, 62.6–95.3)	2/8 (25.0, 3.2–65.1)
Chmait et al. [12], 2010	1998–2008	20 (16–24)	40	26 (65.0)	37/40 (92.5, 79.6–98.4)	92/120 (76.7, 68.1–83.9)	not known
Diemert et al. [13], 2010	2004–2008	20 (17–23)	13	9 (69.2)	11/13 (84.6, 54.5–98.1)	27/36 (75.0, 57.8–87.9)	7/11 (63.6, 30.8–89.1)
Peeters et al. [14], 2012	2000–2012	18 (15–25)	8	4 (50.0)	8/8 (100, 63.1–100)	19/24 (79.2, 57.8–92.9)	4/8 (50.0, 15.7–84.3)
Argoti et al. [15], 2014	2005–2011	20 (15–25)	16	13 (81.2)	16/16 (100, 79.4–100)	39/48 (81.3, 67.4–91.1)	not known
Ishii et al. [16], 2014	2007–2013	21 (16–25)	9	6 (66.7)	9/9 (100, 66.4–100)	20/27 (74.1, 53.7–88.9)	4/9 (44.4, 13.7–78.8)
Our study[a]	1996–2015	18 (15–23)	33	30 (90.9)	32/33 (97.0, 84.2–100)	72/99 (72.7, 62.9–81.2)	22/32 (68.8, 50.0–83.9)
Pooled analysis			132		126/132 (94.4, 90.1–97.6)	301/393 (76.1, 71.9–80.2)	43/73 (56.7, 43.1–69.8)
Cochran's Q (p value)					4.3230 (0.7419)	2.0919 (0.9546)	6.8491 (0.2321)
I^2 statistic, % (95% CI)					0 (0–56.3)	0 (0–56.3)	27 (0–70.7)

GA = Gestational age. [a] Including data from Sepulveda et al. [10].

Table 3. Studies reporting on endoscopic laser surgery for FFTS in MCTA triplet pregnancies

Study	Period	Median GA at laser surgery (range), weeks	Total, n	Stage 3/4, n (%)	Survival of >1 baby, n/total n (%, 95% CI)	Overall survival n/total n (%, 95% CI)	Live birth at <32 weeks, n/total n (%, 95% CI)
De Lia et al. [11], 2009	1992–2008	21 (18–25)	2	1 (50.0)	1/2 (50.0, 1.3–98.7)	3/6 (50.0, 11.8–88.2)	1/2 (50.0, 1.3–98.7)
Chmait et al. [12], 2010	1998–2008	19 (17–22)	6	2 (33.3)	5/6 (83.3, 35.9–99.6)	11/18 (61.1, 35.7–82.7)	4/5 (80.0, 28.4–99.5)
Diemert et al. [13], 2010	2004–2008	19 (18–20)	3	1 (33.3)	2/3 (66.7, 9.4–99.2)	5/9 (55.6, 21.2–86.3)	1/2 (50.0, 1.3–98.7)
Ishii et al. [16], 2014	2007–2013	20 (17–22)	7	4 (57.1)	7/7 (100, 59.0–100)	18/21 (85.7, 63.7–97.0)	5/7 (71.4, 29.0–96.3)
Our study[a]	1996–2015	18 (16–23)	11	11 (100.0)	9/9 (81.8, 48.2–97.7)	11/33 (33.3, 18.0–51.8)	6/9 (66.7, 29.9–92.5)
Pooled analysis			29		24/29 (80.6, 64.9–92.4)	48/87 (57.5, 36.2–77.4)	17/25 (65.4, 47.7–81.1)
Cochran's Q (p value)					4.3804 (0.3570)	15.9245 (0.0031)	0.9285 (0.9204)
I^2 statistic, % (95% CI)					8.7 (0–67.1)	74.9 (6.1–87.9)	0 (0–64.4)

GA = Gestational age. [a] Including data from Sepulveda et al. [10].

Synthesis with Results from Previous Studies

The literature search identified 8 previous studies reporting data on DCTA pregnancies with FFTS treated by endoscopic laser surgery, and the combined data from these studies with ours are shown in table 2 and figure 1 [9–16]. In a total of 132 such pregnancies, the pooled survival rate of at least one baby was 94.4% (95% CI 90.1–97.6), and the overall survival for all babies was 76.1% (95% CI 71.9–80.2); there was no significant heterogeneity between the studies. Delivery in live births at <32 weeks' gestation occurred in 56.7% (95% CI 43.1–69.8) of cases.

The literature search identified 5 previous studies reporting data on MCTA pregnancies with FFTS treated by endoscopic laser surgery, and the combined data from these studies with ours are shown in table 3 and
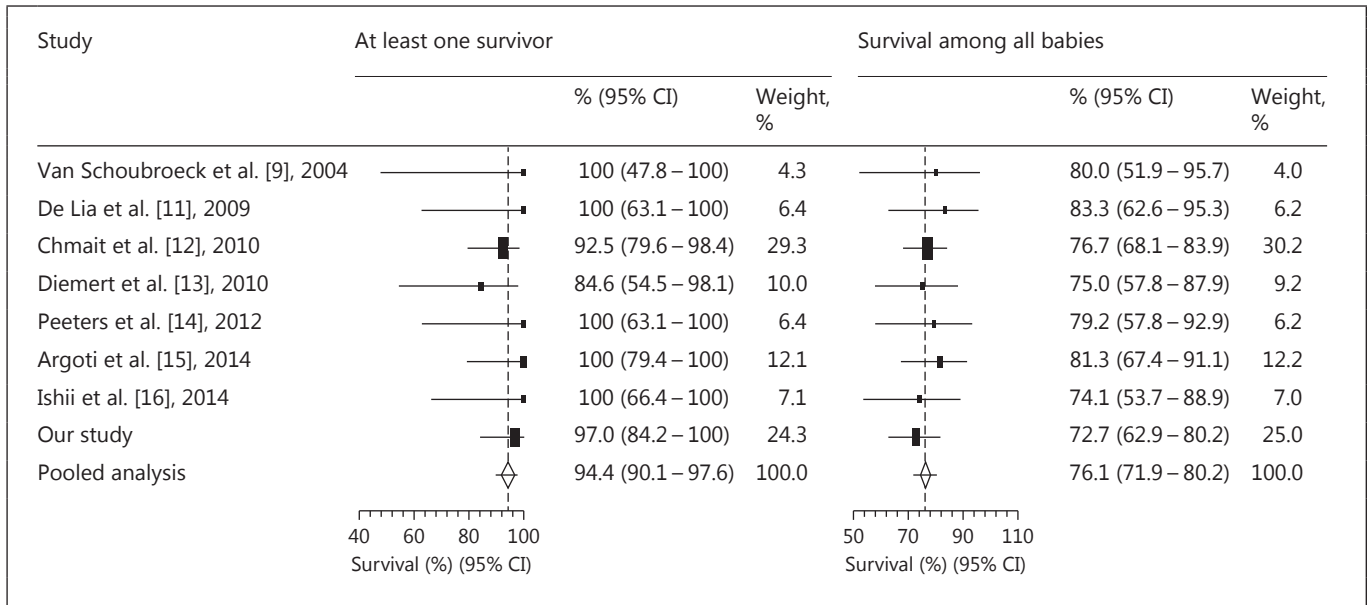
Fig. 1. Pooled estimates of rates of at least one survivor and survival among all babies in DC triplet pregnancies treated with laser coagulation of placental vessels for FFTS.
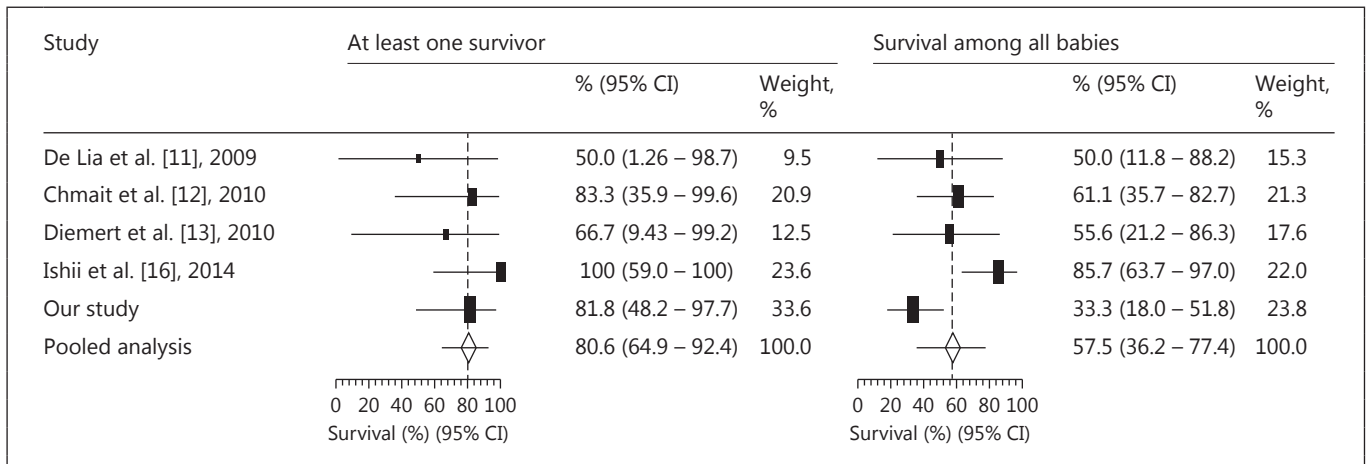

Fig. 2. Pooled estimates of rates of at least one survivor and survival among all babies in MC triplet pregnancies treated with laser coagulation of placental vessels for FFTS.

figure 2 [10–13, 15]. In a total of 29 such pregnancies, the pooled survival rate of at least one baby was 80.6% (95% CI 64.9–92.4), and the overall survival for all babies was 57.5% (95% CI 36.2–77.4); there was significant heterogeneity between the studies. Delivery in live births at <32 weeks' gestation occurred in 65.4% (95% CI 47.7–81.1) of cases.

Discussion

The findings of this study demonstrate the feasibility of endoscopic laser coagulation of communicating placental vessels in the treatment of MC and DC triplet pregnancies complicated by severe FFTS or sFGR. In DC triplets, the separate fetus can pose some technical problems in selecting the appropriate site of entry of the fetoscope, but in

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general, these problems can easily be overcome; consequently, the outcome of affected pregnancies either by FFTS or sFGR is similar to that in MC twins but with an inevitable higher incidence of early preterm birth. In contrast, in MC triplets, endoscopic laser surgery can be technically difficult because of the necessity to coagulate the communicating placental vessels between all three fetuses; as a result of such technical problems or the inability to achieve the objective of complete separation between all fetuses, the outcome is poorer than in DC triplets.

In the combined data from this and previous studies, in DC triplets with FFTS, there was survival of at least one baby in about 95% of pregnancies and survival of 75% of all babies. These results are compatible with those of endoscopic laser surgery in MC twins with severe FFTS. However, in the triplet pregnancies, a very high proportion of survivors, about 60%, were born at <32 weeks' gestation. We have previously reported that in trichorionic triplet pregnancies with three live fetuses at 10–14 weeks' gestation that were managed expectantly, 35% delivered at <33 weeks; the rate in DC triplet pregnancies managed expectantly was 46% [27]. The higher rate of preterm birth in DC triplets complicated by severe FFTS and treated by endoscopic laser surgery is not surprising.

In our DC triplets with sFGR type II, there was survival of at least one baby in 79% of pregnancies and survival of 52% of all babies. These results are compatible with findings in our series of 547 MC twin pregnancies with sFGR type II treated with endoscopic laser surgery; there was survival of at least one baby in 72% of pregnancies, and 54% of all babies survived [7]. However, survival of the growth-restricted fetus in our DC triplets (7%) was lower than in our MC twin pregnancies with sFGR (40%), possibly because the placental territory of the growth-restricted fetus in DC triplets may be smaller than in MC twins.

In the DC triplets with sFGR type II, 46% of survivors were born at <32 weeks' gestation. A likely explanation for this lower rate of early preterm birth than in our DC triplets with FFTS treated with endoscopic laser (46 vs. 69%) is that following laser surgery, 93% of pregnancies with sFGR continued to delivery with only one or two live fetuses, whereas in those with FFTS, the equivalent rate was 54%; consequently, in relation to preterm birth, only 7% in the sFGR group versus 46% in the FFTS group behaved as triplet pregnancies.

In MC triplets with severe FFTS, in comparison to DC triplets with FFTS, survival was poorer. In our MC triplets, at least one baby survived in 82 of the pregnancies, and 39% of all babies survived, compared to the respective rates of 97 and 73% in our series of DC triplets. The number of MC triplets is too small for definite conclusions to be drawn, but it is certain that endoscopic laser surgery in these pregnancies is considerably more difficult than in DC triplets.

The results from endoscopic laser surgery in triplet pregnancies in our series and those from previous smaller studies allow some general conclusions to be drawn on the effectiveness of such therapy and overall survival rates. However, the total number of cases is still too small to allow accurate assessment of outcome according to subgroups of triplets, including MC and DC complicated by FFTS and/or sFGR, different stages of FFTS, gestational age at therapy or techniques of endoscopic laser surgery.

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Disclosure Statement

The authors declare that they have no conflicts of interest.

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