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Stage-based recipient and donor outcome in twin-to-twin transfusion syndrome treated by fetoscopic laser surgery using Solomon technique

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KEYWORDS: donor; equatorial laser; recipient; Solomon laser surgery; survival; TTTS; twin–twin transfusion syndrome

CONTRIBUTION

What are the novel findings of this work?

In an unselected cohort of patients with twin-to-twin transfusion syndrome, primary Solomon laser treatment led to high rates of disease resolution and double twin survival. In the absence of placenta-mediated fetal growth restriction, which is most common in Quintero Stage-III donors, survival chances for both twins were comparable between recipient and donor twins and across Quintero stages.

What are the clinical implications of this work?

Solomon laser treatment should be considered as the primary management option for twin-to-twin transfusion syndrome. Preoperative assessment of placenta-based risks for the donor twin is most relevant for establishing postoperative survival expectations.

ABSTRACT

Objective *To evaluate twin survival stratified by Quintero stage in patients with twin-to-twin transfusion syndrome (TTTS) after Solomon laser treatment.*

Methods *This was a single-center study at Johns Hopkins Center for Fetal Therapy, investigating a cohort of consecutive twin pregnancies treated with the Solomon laser technique for TTTS. Preoperative Quintero stage, perioperative characteristics and obstetric factors were investigated in relation to neonatal survival of the recipient and donor twins at discharge. Determinants of twin survival were evaluated using univariate logistic regression and cumulative survival probability analyses.*

Results *Of 402 pregnancies with TTTS that underwent Solomon laser treatment, 80 (19.9%) were diagnosed with Quintero Stage-I TTTS, 126 (31.3%) with Stage II, 169 (42.0%) with Stage III and 27 (6.7%) with Stage IV. Post-laser twin anemia polycythemia sequence or recurrent TTTS occurred in 19 (4.7%) patients and 11 (2.7%) required repeat laser surgery. Preterm prelabor rupture of membranes occurred in 150 (37.3%) patients and median gestational age at delivery was 32 + 1 weeks. In 303 (75.4%) patients, both twins were alive at discharge; 67/80 (83.8%) were Stage I, 101/126 (80.2%) were Stage II, 113/169 (66.9%) were Stage III and 22/27 (81.5%) were Stage IV ($P = 0.062$). Donor twin survival was lower than that of recipients in cases with Stage-III TTTS (118/169 (69.8%) vs 145/169 (85.8%) ($\chi^2 = 26.076$, $P < 0.0001$)). Higher intertwin size discordance and absent or reversed umbilical artery (UA) end-diastolic velocity (EDV) were associated with donor demise (Nagelkerke R^2, 0.38; $P < 0.001$). Overall, spontaneous post-laser donor demise occurred in 53 (39.6%) patients, accounting for the majority of all losses. Cumulative donor survival decreased from 92% to 65% when intertwin size discordance was >30% and to 48% when UA-EDV was absent or reversed ($P < 0.001$).*

Conclusions *The Solomon laser technique achieves TTTS resolution and double twin survival in a high proportion of cases. Recipient and donor survival is comparable unless there is significant intertwin size discordance and placental dysfunction. This degree of unequal placental sharing, typically found in Stage-III TTTS, is the primary factor preventing double survival due to a higher rate of donor demise.* *© 2024 International Society of Ultrasound in Obstetrics and Gynecology.*

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INTRODUCTION

The presence of placental vascular anastomoses between monochorionic twins can lead to twin-to-twin transfusion syndrome (TTTS)[1], which carries up to 100% twin mortality and morbidity rates when left untreated[2]. The separation of intertwin vascular communications by fetoscopic laser ablation of the connecting anastomoses has become an established first-line therapy for TTTS[3]. This is based on comparative analyses of management strategies performed in randomized or sequential cohorts, as well as single-center studies providing additional insight into outcomes with laser surgery across the spectrum of TTTS disease severity[4]. Consequently, laser surgery has evolved from non-selective[5] to selective coagulation of intertwin anastomoses[6], with optional sequential coagulation[7]. The Solomon technique was developed with the goal of achieving complete functional dichorionization by coagulation of anastomoses and the chorionic plate along the vascular equator[8]. While randomized and observational studies agree on lower recurrence rates after Solomon laser treatment compared with the selective laser technique, there is disagreement on whether survival and morbidity are also improved across the severity spectrum of TTTS[9–12].

The theoretical benefits of more complete dichorionization following Solomon laser therapy should ideally extend beyond lower recurrence rates and include better postoperative recovery of both twins from TTTS, as well as protection from adverse outcomes in the event of single twin demise. This is examined most comprehensively by evaluating individual twin and treatment outcomes stratified according to disease severity, which has been reported only for selective laser therapy[13–15]. Having uniformly offered Solomon laser treatment as a first-line therapy for all TTTS patients at our center, it was our aim in this study to evaluate stage-based twin survival and treatment outcome, and to identify predictors for adverse outcome associated with this technique.

METHODS

We reviewed retrospectively all consecutive twin pregnancies with TTTS referred to the Johns Hopkins Center for Fetal Therapy between July 2014 and March 2023. Patients underwent a detailed ultrasound assessment including measurement of amniotic fluid volume, fetal and maternal Doppler, anatomical survey and fetal echocardiography using high-resolution ultrasound equipment (Voluson E10; GE Healthcare, Zipf, Austria). The diagnosis of TTTS was based on deepest vertical fluid pocket of > 8 cm in the recipient and < 2 cm in the donor. TTTS stage was assigned using the Quintero staging system[6]. In addition, intertwin size discordance, individual fetal weights, individual Doppler findings and cervical length were recorded. The cohort includes all patients with a twin pregnancy between 16 weeks and 27 weeks of gestation who met the criteria for Stage-II TTTS or higher, as well as those with complicated Stage-I disease (amniotic fluid pocket > 10 cm, twin anemia polycythemia sequence (TAPS), preterm contractions or short cervical length < 2.5 cm) that had laser surgery. Final analysis was restricted to patients whose infants had been discharged from inpatient neonatal care. Selective fetal reduction, expectant management or pregnancy termination were offered as alternative treatment options. Concurrent diagnoses, such as selective fetal growth restriction (sFGR) (defined as estimated fetal weight (EFW) < 10^{th} percentile and intertwin EFW discordance > 25%[16]) and cervical shortening, were discussed and managed as appropriate.

Solomon laser surgery was performed by five operators using the previously reported technique, instrumentation and steps to determine optimal access[8,17]. A diode laser (Dornier Med-Tech GmbH, Wessling, Germany) was utilized, and the laser energy was adjusted to achieve coagulation with visual blanching of the communicating vessels and chorionic plate. Complete blanching was defined as vascular collapse obliterating all discernible vascular connection; partial blanching refers to the presence of a residual intravascular clot in the lumen. Sequential coagulation of donor–recipient arteriovenous (AV) anastomoses followed by recipient–donor AV anastomoses was performed, if feasible, when there was coexisting sFGR[7]. The Solomon laser procedure was documented as complete by the surgeon when all anastomoses and the chorionic plate along the vascular equator were coagulated to achieve visual blanching from one placental edge to the other. Anastomosis type and number, quality of visualization, laser energy, procedure times and complications were recorded intraoperatively. Following laser surgery, patients were hospitalized until they were free of contractions. Women underwent an ultrasound scan daily until discharge to assess fetal viability, cervical shortening and the beginning of TTTS resolution. Follow-up ultrasound scans after discharge were performed weekly for 2 weeks and then according to International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines[16] and adjusted according to the clinical picture.

Treatment success was defined as complete resolution of TTTS. Recurrent TTTS or post-laser TAPS were defined by persistence of TTTS criteria or worsening middle cerebral artery peak systolic velocity discordance of at least > 0.5 multiples of the median after 1 week post laser treatment[18].

Double demise was defined as demise of both twins within 48 h of laser surgery and cotwin demise for the second twin if demise occurred later. If demise of one twin occurred, follow-up neurosonography or fetal magnetic resonance imaging was performed on the surviving cotwin. For patients delivering with their referring provider, outcome details were ascertained by research staff and entered into a dedicated Research Electronic Data Capture (REDCap, Fort Lauderdale, FL, USA) database. The identity of the twins at follow-up was determined by a combination of factors, including intrauterine location, EFW, placental cord insertion, associated Doppler findings and amniotic fluid levels, as appropriate. Preterm prelabor rupture of membranes (PPROM) was ascertained and further categorized as procedure-related if it occurred within 2 weeks after laser surgery.

Monoamnionicity was suspected when both twins were in one sac without an intertwin membrane. Predictors and outcomes were available for all included patients.

The primary outcome was survival at discharge from the neonatal intensive care unit or nursery, stratified according to Quintero stage. Secondary outcomes were also stratified according to Quintero stage and included survival at 48 h after laser surgery, survival to delivery, survival of the recipient and donor, post-laser TTTS or TAPS recurrence and obstetric outcomes including PPROM. Gestational age at birth and circumstances of delivery were also stratified by Quintero stage.

Statistical analyses were performed using R (www.r-project.org) and Rstudio IDE (www.rstudio.com), and SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Fisher's exact test and the chi-square test were used to compare the proportional distribution of primary and secondary outcomes in pregnancies stratified according to Quintero stage. The Kruskal–Wallis test and Mann–Whitney *U*-test were used for group comparisons of continuous variables stratified according to Quintero stage and recipient *vs* donor twin. Predictors for spontaneous fetal demise of individual twins were first identified by univariate analysis, with the addition of receiver-operating-characteristics (ROC)-curve analysis to identify predictive cut-offs for continuous variables found to be significant. To identify primary determinants, multivariable logistic regression analysis, utilizing significant individual variables as independent variables and fetal demise as the dependent variable, was performed. For all parameters, $P < 0.05$ was considered statistically significant after Bonferroni correction for multiple comparisons. The study protocol was approved by the institutional review board at the Johns Hopkins University.

RESULTS

During the study period, of 433 twin pregnancies with TTTS that were eligible for laser surgery, 420 (97.0%) underwent Solomon laser therapy, of whom 402 met the study inclusion criteria (Figure 1, Table 1). Eighty (19.9%) patients were diagnosed with Quintero Stage-I TTTS, 126 (31.3%) with Stage II, 169 (42%) with Stage III and 27 (6.7%) with Stage IV. The rate of double survival was 88.3% ($n = 355$) at 48 h after laser therapy, 78.4% ($n = 315$) at delivery and 75.4% ($n = 303$) at discharge. Double survival at any timepoint was 9–15% lower for Stage-III TTTS ($\chi^2 = 14.482, P < 0.005$) and the rate of double survival at discharge was lowest for Stage-III TTTS ($P = 0.02$) (Figure 2, Table 2). Furthermore, while recipient twin survival was similar across all Quintero stages, donor twin survival at discharge was significantly lower for Stage-III TTTS ($\chi^2 = 19.168$, $P = 0.0003$) (Figure 2). Accordingly, at discharge, Stage-III donor twins were less likely to survive compared with the recipient twin (118 (69.8%) *vs* 145 (85.8%); $\chi^2 = 26.076$, $P < 0.0001$) (Table 2, Figure 2).

The distribution of gestational age at laser surgery, maximum amniotic fluid pocket for the donor and preoperative EFW discordance differed significantly between Quintero stages (Kruskal–Wallis, $P < 0.001$ for all). Laser surgery was conducted earlier in TTTS Stages II and III (median, 19 + 1 (interquartile range (IQR), 17 + 6 to 21 + 5) weeks) compared with Stages I and IV (median, 22 + 0 (IQR, 19 + 4 to 24 + 2) weeks). In patients with Stage-III TTTS, compared to all other stages of TTTS, donor maximum amniotic fluid vertical pocket was lower (median, 0.7 (IQR, 0–1.4) cm *vs* 1.4 (IQR, 0.9–1.7) cm) and intertwin preoperative size discordance (EFW) was higher (median, 24% (IQR, 15–33%) *vs* 18% (IQR, 9–25%)).

Complete visualization of the vascular equator required manipulation of an overlying twin in 15 (3.7%) procedures, and complete blanching was not achieved in 20 (5.0%) procedures. Solomon laser surgery was assessed to be complete in 362 (90.0%) patients and was performed sequentially in 58 (14.4%) patients for coexisting sFGR of the donor twin.

Postoperative complications included chorioamniotic membrane separation (CAS) ($n = 58$ (14.4%)), and progression to functional monoamnionicity ($n = 35$ (8.7%)) due to incidental or deliberate septostomy in 36 (9.0%) patients. Within 2 weeks after surgery, 18 (4.5%) patients had PPROM, 17 (4.2%) had previable preterm birth and 14 (3.5%) had post-laser pregnancy termination. In 19 (4.7%) patients, there was recurrent TTTS or TAPS, requiring repeat surgery in 11 (2.7%).

Median gestational age at delivery was similar across all Quintero stages and was 32 + 1 weeks of gestation for the whole cohort. The median laser-to-delivery interval was longest for Stage II (13 + 0 (IQR, 8 + 6 to 15 + 4) weeks). Rates of PPROM and placental abruption were also similar across Quintero stages and occurred

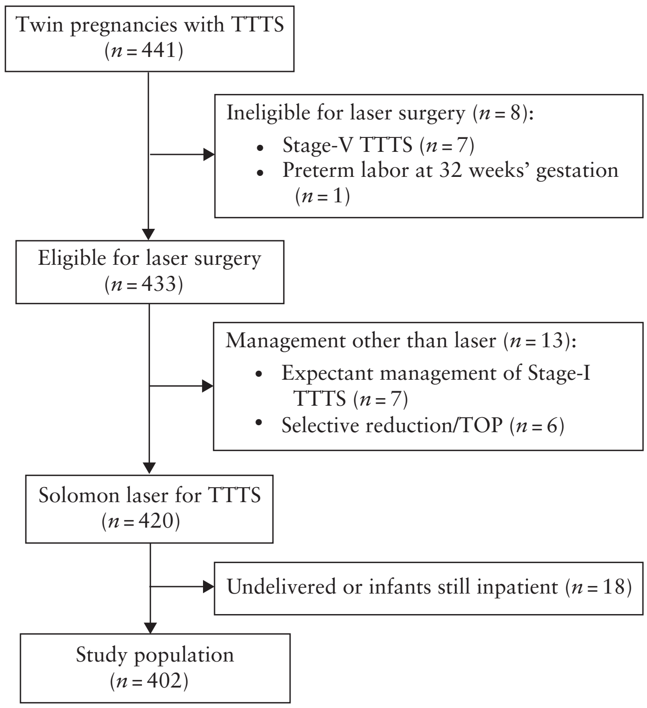


Figure 1 Flowchart of eligible twin pregnancies that underwent Solomon laser therapy for twin-to-twin transfusion syndrome (TTTS). TOP, termination of pregnancy.

Table 1 Maternal and perioperative characteristics of 402 twin pregnancies with twin-to-twin transfusion syndrome (TTTS) that underwent Solomon laser surgery

Parameter	*Value*
Maternal age (years)	31 (28–34)
Maternal race	
White	299 (74.4)
Black	44 (10.9)
Hispanic	37 (9.2)
Asian	20 (5.0)
Other	2 (0.5)
Maternal BMI (kg/m^2)	28.3 (24.0–33.2)
Nulliparous	189 (47.0)
Conception by IVF	49 (12.2)
Prior preterm birth	22 (5.5)
Preoperative CL (mm)	37.7 (32.0–43.2)
Preoperative CL < 15 mm	18 (4.5)
Pessary or cerclage for cervical shortening	64 (15.9)
Pre-laser	14 (3.5)
Post-laser	50 (12.4)
Maximum vertical AF pocket (cm)	
Recipient twin	10.3 (8.9–12.1)
Donor twin	0.9 (0.0–1.5)
Intertwin fetal weight discordance (%)	20 (11–28)
Intertwin fetal weight discordance > 25%	134 (33.3)
TTTS Quintero stage	
Stage I	80 (19.9)
Stage II	126 (31.3)
Stage III	169 (42.0)
Stage IV	27 (6.7)
Anterior placenta	193 (48.0)
GA at laser surgery (weeks)	19 + 1 (18 + 1 to 22 + 2)
Transplacental trocar insertion	17 (4.2)
Solomon laser completed successfully	362 (90.0)
Sequential laser technique	58 (14.4)
Intraoperative amnioinfusion volume (mL)	500 (0–1000)
Amniodrainage (mL)	1550 (1100–2150)
Complete visualization of intertwin anastomoses	383 (95.3)
Number of coagulated intertwin anastomoses	15 (10–21)
Coagulation achieved complete blanching	382 (95.0)
Maximum laser power used (W)	30 (20–30)
Total laser energy (J)	7807 (5315–11 915)
Laser deployment time (min)	6.2 (4.4–8.3)
Total operative time (min)	54 (41–66)

Data are given as median (interquartile range) or *n* (%). AF, amniotic fluid; BMI, body mass index; CL, cervical length; GA, gestational age; IVF, *in-vitro* fertilization.

in 150 (37.3%) and 15 (3.7%) patients, respectively. While recipient birth weight was similar across Quintero stages, donor birth weight was lowest in those with Stage-III TTTS, resulting in significantly higher intertwin size discordance for Stage-III pregnancies with double survival (Table 2).

There were 52 recipient and 82 donor losses, resulting in 134 twin losses overall. Spontaneous post-laser demise of the donor twin accounted for the majority ($n = 53$ (39.6%)) (Table 3) of all losses, and in seven patients there was associated subsequent cotwin demise of the recipient, accounting for an additional 5.2% of all losses. Selective reduction (two recipients, one donor), termination of pregnancy (nine recipients, eight donors), previable preterm birth (10 recipients, nine donors) and neonatal death (10 recipients, 11 donors) contributed comparably to the loss rate. The high rate of spontaneous post-laser donor demise was responsible for the significant difference in the causes of twin loss for recipient and donor twins ($\chi^2 = 27.0404$, $P = 0.0006$). There was no case of abnormal brain imaging in surviving cotwins.

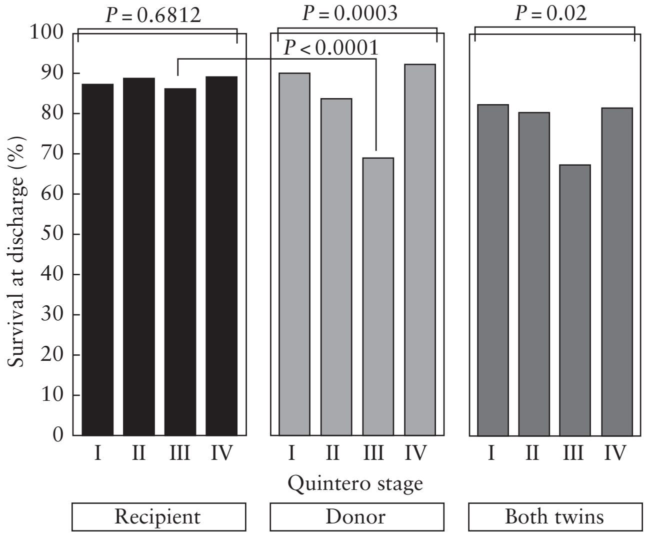


Figure 2 Bar charts demonstrating survival rates for recipient and donor twins as well as double twin survival, stratified according to twin-to-twin transfusion syndrome (TTTS) Quintero stage. While recipient survival was similar across Quintero stages, donor survival was lower in those with Stage-III TTTS, contributing to a lower double twin survival rate for this stage. All *P*-values indicate chi-square tests.

Logistic regression did not identify a determining predictor for recipient twin demise. In contrast, spontaneous post-laser donor demise was determined by absent or reversed umbilical artery (UA) end-diastolic velocity (EDV), intertwin size discordance > 30%, anterior placentation or laser deployment time > 8 min utilized for coagulation (Nagelkerke R^2, 0.38; $P < 0.001$) (Table 4). Quintero stage was not independently predictive for donor demise. Comparable cumulative survival with the recipient twin decreased progressively and significantly for the donor twin in the presence of > 30% size discordance and absent or reversed UA-EDV (Breslow $\chi^2 = 77.432$, $P < 0.001$) (Figure 3).

DISCUSSION

We conducted a large Quintero stage-based single-center analysis of TTTS treated with the Solomon laser technique. Except in cases of Quintero Stage-III TTTS, recipients and donors had a comparable survival rate and a double survival rate exceeding 80%. Severe growth restriction and placental dysfunction evidenced by abnormal Doppler were the primary contributors to

Table 2 Pregnancy outcome overall and according to Quintero stage in 402 twin pregnancies that underwent Solomon laser surgery for twin-to-twin transfusion syndrome

Outcome	*All patients (N = 402)*	*Stage I (n = 80)*	*Stage II (n = 126)*	*Stage III (n = 169)*	*Stage IV (n = 27)*	P
Survival at 48 h						0.075
Double	355 (88.3)	74 (92.5)	117 (92.9)	139 (82.2)	25 (92.6)	
Single	43 (10.7)	5 (6.3)	9 (7.1)	27 (16.0)	2 (7.4)	
None	4 (1.0)	1 (1.3)	0 (0)	3 (1.8)	0 (0)	
PPROM*	150 (37.3)	27 (33.8)	58 (46.0)	57 (33.7)	8 (29.6)	0.105
GA at delivery (weeks)	32 + 1 (28 + 6 to 34 + 2)	32 + 6 (29 + 3 to 34 + 4)	32 + 1 (28 + 4 to 34 + 0)	31 + 5 (28 + 4 to 34 + 2)	33 + 5 (29 + 2 to 35 + 1)	0.175
Laser-to-delivery interval (weeks)	11 + 6 (8 + 0 to 14 + 7)	10 + 4 (7 + 1 to 13 + 3)	13 + 0 (8 + 6 to 15 + 4)	11 + 6 (8 + 6 to 15 + 0)	10 + 0 (5 + 5 to 13 + 6)	0.019
Placental abruption	15 (3.7)	6 (7.5)	3 (2.4)	5 (3.0)	1 (3.7)	0.253
Delivery details						0.267
TOP	14 (3.5)	1 (1.3)	2 (1.6)	11 (6.5)	0 (0)	
Previable preterm birth	17 (4.2)	4 (5.0)	7 (5.6)	6 (3.6)	0 (0)	
CS	290 (72.1)	58 (72.5)	94 (74.6)	117 (69.2)	21 (77.8)	
Vaginal delivery	80 (19.9)	16 (20.0)	23 (18.3)	35 (20.7)	6 (22.2)	
CS for second twin	1 (0.2)	1 (1.3)	0 (0)	0 (0)	0 (0)	
Recipient twin BW (g)	1830 (1350–2240)	1935 (1355–2322)	1800 (1425–2214)	1770 (1280–2220)	1965 (1280–2220)	0.506
Donor twin BW (g)	1575 (1010–1997)	1670 (1202–2109)	1670 (1205–2055)	1453 (878–1900)	1609 (1055–2204)	0.022
BW discordance† (%)	9 (3–19)	9 (3–19)	7 (3–15)	12 (6–28)	8 (2–20)	0.004
1-min Apgar score						
Recipient twin	7 (6–8)	7 (5–8)	8 (5–8)	7 (6–8)	8 (7–8)	0.605
Donor twin	7 (5–8)	7 (5–8)	7 (5–8)	7 (5–8)	7 (5–8)	0.296
5-min Apgar score						
Recipient twin	9 (8–9)	8 (8–9)	9 (8–9)	9 (8–9)	9 (8–9)	0.899
Donor twin	9 (8–9)	9 (8–9)	9 (8–9)	9 (8–9)	9 (8–9)	0.992
Survival at birth						
Recipient twin	360 (89.6)	71 (88.8)	115 (91.3)	150 (88.8)	24 (88.9)	0.355
Donor twin	331 (82.3)	74 (92.5)	111 (88.1)	121 (71.6)	25 (92.6)	0.003
Double	315 (78.4)	69 (86.3)	106 (84.1)	118 (69.8)	22 (81.5)	0.015
Single	61 (15.2)	7 (8.8)	14 (11.1)	35 (20.7)	5 (18.5)	
None	26 (6.5)	4 (5.0)	6 (4.8)	16 (9.5)	0 (0)	
Survival at discharge						
Recipient twin	351 (87.3)	70 (87.5)	112 (88.9)	145 (85.8)	24 (88.9)	0.6812
Donor twin	321 (79.9)	72 (90.0)	106 (84.1)	118 (69.8)	25 (92.6)	0.0003
Double	303 (75.4)	67 (83.8)	101 (80.2)	113 (66.9)	22 (81.5)	0.062
Single	66 (16.4)	8 (10.0)	16 (12.7)	37 (21.9)	5 (18.5)	
None	33 (8.2)	5 (6.3)	9 (7.1)	19 (11.2)	0 (0)	

Data are given as *n* (%) or median (interquartile range). *Cases of preterm prelabor rupture of membranes (PPROM) at any time after procedure. †Calculated for pregnancies with double survival only. BW, birth weight; CS, Cesarean section; GA, gestational age; TOP, termination of pregnancy.

post-laser donor demise, and were ultimately responsible for the lower rate of Stage-III double survival. Solomon laser treatment was considered complete intraoperatively in 90% of cases, and the high likelihood of functional dichorionization is illustrated by less than 3% of patients requiring repeat intervention and no case of cotwin organ damage attributable to single twin demise. PPROM, both related (≤ 2 weeks) and unrelated (> 2 weeks) to the procedure, and early delivery were the primary obstetric complications in almost half of the pregnancies.

A primary stage-based survival analysis stratified according to recipient and donor status has been reported for selective[15] and sequential[13] laser ablation. Bamberg *et al.* reported double twin survival of 69.0%, 71.4%, 55.4% and 51.0% cases of TTTS Quintero Stage I, II, III and IV, respectively[15]. Recipient survival was 10% higher compared with donors, except in Stage-IV TTTS, in which it was 10% lower. Chmait *et al.*[13] performed sequential selective laser for coexisting fetal growth restriction and reported similar survival trends across Quintero stages to those of Bamberg *et al.*[15], but noted a 5–17% higher rate of stage-based double survival[13]. Three systematic reviews compared outcomes between Solomon and selective laser therapy[12,19,20]. In a non-pooled meta-analysis, only observational studies demonstrated a higher survival rate of at least one twin, while the randomized controlled trial (RCT) demonstrated only a reduction in TAPS and TTTS recurrence when using the Solomon compared

Table 3 Characteristics of twins that underwent spontaneous demise or survived after laser surgery for twin-to-twin transfusion syndrome, according to recipient or donor status, excluding cases of selective reduction and pregnancy termination

	Recipient twin			*Donor twin*		
Characteristic	*Survivor (n = 382)*	*Demise (n = 20)*	P	*Survivor (n = 349)*	*Demise (n = 53)*	P
GA at laser (weeks)	19 + 5 (18 + 0 to 22 + 2)	20 + 2 (18 + 6 to 22 + 1)	0.319	20 + 0 (18 + 1 to 22 + 3)	19 + 2 (18 + 0 to 21 + 6)	0.322
Anterior placenta	179 (46.9)	12 (60.0)	0.265	159 (45.6)	34 (64.2)	0.012
Intertwin size discordance (%)	20 (11–27)	19 (10–33)	0.680	19 (10–26)	30 (19–37)	<0.001
Maximum vertical AF pocket (cm)	10.2 (9.1–12.4)	10.9 (8.7–13.2)	0.497	0.9 (0–1.5)	1 (0.2–1.8)	0.133
UA-AREDV	10 (2.6)	1 (5.0)	0.530	56 (16.0)	31 (58.5)	<0.001
MCA-PSV MoM	1.04 (0.89–1.19)	1.03 (0.91–1.13)	0.378	1.07 (0.92–1.27)	1.20 (1.00 –1.45)	0.005
MCA-PSV MoM discordance	0.01 (−0.18 to 0.27)	0.08 (−0.28 to 0.55)	0.749	0 (−0.19 to 0.25)	0.15 (−0.70 to 0.48)	0.002
Ductus venosus RAV	76 (19.9)	4 (20.0)	0.955	12 (3.4)	5 (9.4)	0.044
Umbilical venous pulsations	108 (28.5)	4 (20.0)	0.410	35 (10.1)	6 (11.3)	0.777
Hydrops	26 (6.8)	1 (5.0)	0.806	0 (0)	0 (0)	—
Intraoperative characteristics						
Amnioinfusion volume (mL)	500 (0–1000)	450 (0–1000)	0.968	413 (0–1000)	900 (475–1250)	<0.001
Amnioreduction volume (mL)	1550 (1100–2200)	1900 (1463–2438)	0.200	1600 (1113–2200)	1450 (835–2225)	0.321
Amnioreduction time (min)	8 (5–10)	6 (0–9)	0.300	8 (5–11)	8 (5–10)	0.780
Total fetoscopy time (min)	53 (41–65)	60 (46–86)	0.020	53 (40–64)	60 (47–74)	0.008
Maximum power used (W)	30 (20–30)	30 (30–35)	0.002	30 (20–30)	30 (30–30)	0.006
Maximum energy used (J)	7762 (5316–11863)	9589 (5016–13750)	0.400	7603 (5284–11335)	11250 (5420–16403)	0.016
Laser deployment time (min)	6.2 (4.4–8.3)	6.8 (4.6–9.6)	0.588	6.1 (4.4–8.1)	8.2 (4.3–11.1)	0.008
Number of placental anastomoses						
Total	15 (10–21)	17 (12–22)	0.356	15 (10–21)	15 (10–22)	0.650
Artery-to-vein	9 (6–14)	12 (6–15)	0.386	10 (6–14)	9 (6–14)	0.698

Data are given as median (interquartile range) or *n* (%). AF, amniotic fluid; GA, gestational age; MCA, middle cerebral artery; MoM, multiples of the median; PSV, peak systolic velocity; RAV, reversed or absent a-wave; UA-AREDV, umbilical artery absent or reversed end-diastolic velocity.

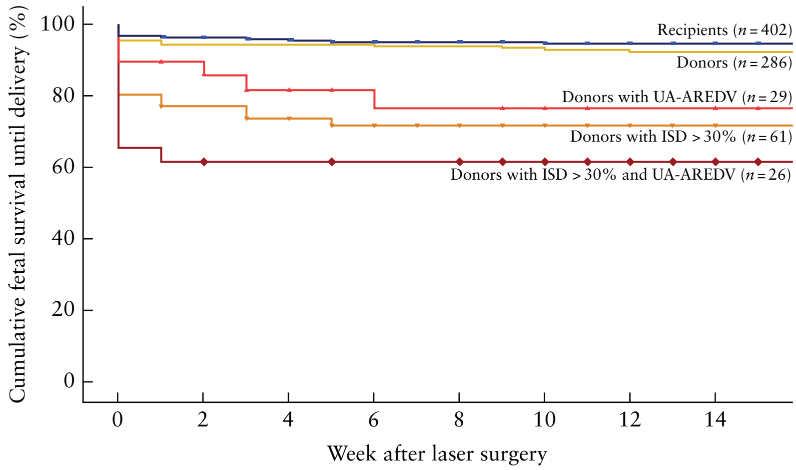
Table 4 Predictors of spontaneous donor demise after laser surgery for twin-to-twin transfusion syndrome

Variable	*AUC (95% CI)*	*OR (95% CI)*	P
UA-AREDV	NA	7.709 (3.658–16.246)	< 0.001
Laser deployment > 8 min	0.617 (0.518–0.716)	4.368 (2.177–8.764)	< 0.001
Intertwin size discordance > 30%	0.713 (0.630–0.795)	3.118 (1.509–6.444)	0.002
Anterior placenta	NA	3.039 (1.468–6.294)	0.003

AUC, area under the receiver-operating-characteristics curve; NA, not applicable; OR, odds ratio; UA-AREDV, umbilical artery absent or reversed end-diastolic velocity.

to the selective technique[12]. Two pooled meta-analyses concluded that Solomon laser surgery resulted in higher survival for the recipient, for both twins and at least one twin. There was a 57% reduction in TTTS recurrence but the risk for placental abruption was increased and delivery was at an earlier gestational age[19,20]. These meta-analyses do not include the large single-center study of Bartin *et al.* that demonstrated a higher survival rate and lower rate of post-laser TAPS, but a higher PPROM rate and earlier delivery in cases treated with the Solomon technique compared to a matched cohort treated with selective laser[21]. In comparison with the Quintero stage-based selective laser studies of Chmait *et al.*[13] and Bamberg *et al.*[15], our recipient survival was 13% and 18% higher in patients with Stage-III and -IV TTTS, respectively, and 5–17% higher for donors across all stages, resulting in a 7–21% higher stage-based double survival rate. Based on available comparable information, our double and single survival rates also compare favorably with other Solomon laser cohorts[8,9,11,22–26].

In addition to the surgical technique, survival can depend on specific case selection, obstetric outcomes and prematurity rate. In our study, almost all eligible patients elected laser surgery. Moreover, Quintero stage severity, perioperative characteristics, complication rates and gestational age at delivery were comparable to prior studies[9,13,15]. These factors are therefore unlikely to have contributed to the differences in survival rates seen in our study compared with previous publications. While concern has been raised that Quintero staging does not accurately reflect recipient compromise[27], most of our recipient twins survived and we only identified predictors for donor demise. These predictors include intertwin size discordance and UA Doppler, which reflects



Fetal demises

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Number of all fetuses at risk	754	747	746	741	740	737	735	735	735	734	732	732	731	731	731
Number of fetal demises:															
Recipients	13	1		2	1	2					1				
Donors	13	3					1			1	1		1		
Donors with UA-AREDV	3		1	1			1								
Donors with ISD > 30%	12	2		2		1									
Donors with UA-AREDV & ISD > 30%	9	1													

Figure 3 Kaplan–Meyer curves showing cumulative fetal survival probability for recipient and donor twins in the weeks after Solomon laser surgery. Donor twins are presented in four subsets: no additional risk factors, presence of absent or reversed umbilical artery end-diastolic velocity (UA-AREDV), intertwin size discordance (ISD) > 30% and UA-AREDV with concurrent size discordance > 30%. The table enumerates fetal demise per week after laser surgery for recipient twins and each subset of donor twins, as well as the total number of twins at risk.

unequal placental sharing and the degree of vascular dysfunction in the placental territories. This observation is consistent with other studies[22–24,26,28] and a recent meta-analysis that recognized coexisting sFGR as one of the primary factors limiting post-laser double survival[29]. One potential explanation for higher rates of survival after Solomon laser surgery is the lower number of residual anastomoses and more extensive fibrosis of the shared cotyledons that constitute the 'third circulation' of the placenta than is achievable by selectively coagulating anastomoses[30–33]. This would not only normalize volume imbalance[34] but limit the transfer of vasoactive substances and metabolites that contribute to TTTS severity, thus facilitating post-laser recovery[35,36].

The potential benefits of Solomon laser surgery should be weighed against the risks of placental abruption and PPROM, currently attributed to placental and membrane damage as a result of the higher laser energy[20,33]. A large meta-analysis reported placental abruption in 6% of Solomon and 2% of selective laser surgeries, with rates of PPROM of 22% and 18% in the respective groups[20]. There are several obstacles to identifying reliable strategies to mitigate these risks. Laser types, settings and energy use are not reported uniformly[20,33]. Over 10% of patients experience intrauterine bleeding intraoperatively from various sources[9,22–24], subsequently presenting with antepartum hemorrhage often attributed clinically to placental abruption without detailed placental analysis[33,37]. During laser surgery, we used 2000 J less than in the selective laser cohort in one study[23] and 1500 J less than that used in the Solomon laser cohort of a RCT[9], achieving similar therapeutic efficiency and histologically confirmed placental abruption in 3.7%. The complication rates (PPROM, septostomy, functional monoamnionicity or CAS) and gestational age at delivery in our study are comparable to those reported in the literature and is potentially attributable to the fact that over 75% of pregnancies continued with two live fetuses. Recognizing that twin pregnancies have approximately twice the PPROM rate compared with singleton pregnancies and a shorter latency-to-delivery interval when PPROM occurs[38] emphasizes the need for strategies to improve these statistics if laser leads to a higher rate of double survivors[39].

Limitations of the present study include the lack of a control group treated with selective laser to provide a direct stage-based outcome comparison between the Solomon and selective laser techniques. The retrospective study design limits the availability of detailed obstetric outcome data or standardized placental pathology to provide information on post-laser vascular architecture or additional histological features, such as placental damage or placental abruption. Unfortunately, beyond neonatal survival we have inconsistent data on neonatal complications which does not allow us to quantify prematurity-related impact. Strengths of the study include the sample size, capture of detailed prenatal core outcome variables for individual twins, a Quintero stage-based analytical approach and a patient population representative of previous randomized and observational studies allowing us to report additional insights into the benefits of the Solomon laser technique.

In conclusion, we present the outcomes of a large cohort of twin pregnancies with TTTS undergoing Solomon laser as the first-line treatment. The Solomon laser technique, despite its obstetric risk profile, provides both twins with the highest likelihood of functional placental dichorionization, allowing recovery and survival irrespective of TTTS severity. In the absence of significant placental dysfunction, survival of the donor and recipient twin were comparable. When there is growth restriction due to unequal sharing of functional placental territories, donor survival depends on the magnitude of size discordance and placental dysfunction.

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