D'Antonio Francesco (Orcid ID: 0000-0002-7546-8025)
Khalil Asma (Orcid ID: 0000-0003-2802-7670)

Solomon technique *vs* selective fetoscopic laser photocoagulation for twin–twin transfusion syndrome: systematic review and meta-analysis of maternal and perinatal outcomes

F. D'Antonio[1], M. Herrera[2,3], L. Oronzii[1] and A. Khalil[4,5,6]

[1]Center for Fetal Care and High-Risk Pregnancy, University of Chieti, Chieti, Italy

[2]Maternal Fetal Medicine Department, Colsanitas Clinic, Colombian University Clinic - Pediatric Clinic, Bogota, Colombia

[3]Maternal Fetal Medicine Foundation, Fetal Health Foundation, Bogota, Colombia

[4]Fetal Medicine Unit, Saint George's Hospital, London, UK

[5]Vascular Biology Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK

[6]Fetal Medicine Unit, Liverpool Women's Hospital, University of Liverpool, Liverpool, UK

Corresponding author: Prof. A. Khalil

Fetal Medicine Unit, Department of Obstetrics and Gynaecology, St. George's University Hospitals NHS Foundation Trust, Blackshaw Road, London SW17 0QT, UK

E-mail: akhalil@sgul.ac.uk

Short title: Solomon technique versus selective laser for TTTS

Keywords: Solomon technique; selective; fetoscopic; laser; twin-twin transfusion syndrome; TAPS; twin anemia polycythemia sequence; recurrence; rupture of membranes; perinatal loss; survival; preterm birth; systematic review; meta-analysis; outcomes

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/uog.26095

CONTRIBUTION

What are the novel findings of this work?

Despite its recognized role in reducing the risk of recurrent TTTS and TAPS, several recent reports have highlighted the higher risk of placental damage in pregnancies treated with Solomon technique, which can translate into a higher risk of preterm rupture of the membranes (PPROM), placental abruption and shorter treatment to delivery interval.

What are the clinical implications of this work?

Monochorionic twin pregnancies complicated by TTTS undergoing laser treatment using the Solomon technique had a higher survival rate and lower rate of recurrent TTTS, but an increased risk of placental abruption compared to those treated with selective coagulation of placental anastomoses.

ABSTRACT

Objective: To ascertain the maternal and perinatal outcomes of twin pregnancies complicated by twin-twin transfusion syndrome (TTTS) undergoing Solomon technique compared to selective Laser photocoagulation of the placental anastomoses.

Methods: Medline, Embase and Cochrane databases were searched. The outcomes observed were perinatal loss and survival, preterm pre-labor rupture of the membranes (PPROM), preterm birth (PTB), gestational age (GA) at delivery, interval between laser and delivery, maternal bleeding, septostomy or chorioamniotic separation, placental abruption, twin anemia polycythemia sequence (TAPS), recurrence of TTTS, neonatal morbidity and neurological morbidity. Random effect head-to-head meta-analyses were used to analyze the data. Pooled odds ratios (OR) and mean difference (MD) and their 95% confidence intervals (CI) were calculated.

Results: Nine studies were included. There was generally no difference in the main maternal and pregnancy characteristics between pregnancies treated using the Solomon technique and those treated using selective photocoagulation of the placental anastomoses. Twin pregnancies treated using the Solomon technique had a significantly lower birthweight discordance (pooled MD -2.661, 95% CI -3.978 to -1.344; p=0.001). The risk of fetal loss (pooled OR 0.69, 95% CI 0.50-0.95; p=0.023), neonatal (pooled OR 0.35, 95% CI 0.16-0.84; p=0.018) and perinatal (pooled OR 0.56, 95% CI 0.38-0.83; p=0.004) were significantly lower in pregnancies treated using the Solomon technique compared to selective laser coagulation. Likewise, pregnancies treated using the Solomon technique had a significantly higher chance of survival of at least one twin (pooled OR 1.90, 95% CI 1.2-2.3; p=0.004) and double survivors (pooled OR 1.83, 95% CI 1.2-2.7; p=0.002).

There was no difference in the risk of PPROM (p=0.735), PPROM within 10 days from the laser surgery (P=0.982), PTB (p=0.207), maternal bleeding (p=0.322), septostomy or chorioamniotic separation (p=0.670), and chorioamnionitis (p=0.135) between the two groups, while the risk of placental abruption was higher in pregnancies treated using the Solomon technique (pooled OR 2.93, 95% CI 1.6-5.5; p=0.001). In the Solomon technique group,

pregnancies delivered at significantly earlier GA compared to those with selective laser (pooled MD -0.625 weeks, 95% CI -0.90 to -0.35, p<0.001), while there was no difference in the interval between laser and delivery (p=0.589). Recurrence of TTTS was significantly lower in pregnancies undergoing Solomon technique (pooled OR 0.43, 95% CI 0.24-0.91; p<0.001), while there was no difference in the risk of TAPS between the two groups (p=0.792). Finally, there was no difference in the overall risk of neonatal morbidity (p=0.382) and neurological morbidity (p=0.247) between the two groups.

Conclusion: Monochorionic twin pregnancies complicated by TTTS undergoing laser treatment using the Solomon technique had a significantly higher survival rate and lower recurrence rate of TTTS, but an increased risk of placental abruption compared to those treated with selective coagulation of placental anastomoses.

INTRODUCTION

Twin to twin transfusion syndrome (TTTS) is the main determinant of perinatal mortality and morbidity in monochorionic diamniotic (MCDA) twin gestations, complicating 9-15% of these pregnancies[1-6]. TTTS is a hemodynamic condition characterized by relative hypovolemia in the donor and hypervolemia in the recipient secondary to chronic unbalanced flow through the arteriovenous anastomoses. Monitoring for TTTS is essential in order to optimize perinatal outcome1,[2]. Laser photocoagulation of placental anastomoses is the gold standard treatment for pregnancies complicated by advanced TTTS (Quintero stage 2 or symptomatic stage 1). A randomized controlled trial published in 2005 comparing laser vs amnioreduction for the treatment of TTTS reported a higher likelihood of the survival of at least one twin to 28 days of age and 6 months of age in pregnancies treated with laser[7]. Furthermore, infants in the laser group also had a lower incidence of cystic periventricular leukomalacia and were more likely to be free of neurologic complications at six months of age[7].

The original laser technique implied photocoagulation of all anastomoses crossing the intertwin membrane[8]. This technique was subsequently refined to selective photocoagulation, where only pathological intertwin anastomoses were coagulated[9]. More recently, a selective sequential technique, in which the arteriovenous anastomoses from the donor to the recipient are treated first with laser ablation, was introduced[10]. However, several studies reported that after standard fetoscopic laser technique, patent anastomoses were seen in up to one third of the placentas[11]. In order to overcome these potential limitations, several alternatives to conventional coagulation of arteriovenous anastomoses have been reported in recent years. Among them, the Solomon technique has emerged as one of the most promising alternatives to the original laser technique. Solomon technique consists in drawing a thin photocoagulation line with the laser from one placental edge to the other connecting the laser dots. The rationale of this method is to ablate any residual micro-anastomoses and separates the vascular territory of each twin, minimizing the risk of residual anastomoses[12].

The clinical usefulness of Solomon technique compared to conventional ("selective") laser coagulation of placental anastomoses has been addressed in a multicenter randomized controlled trial (RCT). The authors reported that the occurrence of a composite outcome including, twin anaemia polycythaemia sequence (TAPS), recurrence of TTTS, perinatal mortality, or severe neonatal morbidity were lower in pregnancies treated with Solomon technique compared to selective laser coagulation of the placental anastomoses, while there was no difference in the incidence of perinatal mortality and severe neonatal morbidity between the two groups[13]. Despite its recognized role in reducing the risk of recurrent TTTS and TAPS, several recent reports have highlighted the higher risk of placental damage in pregnancies treated with Solomon technique, which can translate into a higher risk of preterm rupture of the membranes (PPROM), placental abruption and shorter treatment to delivery interval.

The aim of this systematic review and meta-analysis was to ascertain the maternal and perinatal outcome of MCDA twin pregnancies complicated by TTTS undergoing Solomon technique compared to selective photocoagulation of the placental anastomoses.

METHODS

Protocol, information sources and literature search

This review was performed according to an a-priori designed protocol and recommended for systematic reviews and meta-analysis[14,15]. Medline, Embase and Cochrane databases were searched electronically on 24th March 2022 utilizing combinations of the relevant medical subject heading (MeSH) terms, key words, and word variants for “twin twin" or "twin to twin" or TTTS or "feto fetal" or "intrauterine cross" or "intra uterine cross" or intertwin or "inter twin" (Table S1). The search and selection criteria were restricted to English language. Reference lists of relevant articles and reviews were hand searched for additional reports. Prisma guidelines were followed[16].

Outcomes measures, study selection and data collection

The outcomes observed were:

- Fetal loss, including miscarriage and intra-uterine death (IUD)
- Neonatal death (NND), defined as death up to 28 days of life
- Perinatal loss, including both fetal loss and neonatal death
- Survival of at least one twin
- Both survivors
- No survivor
- Donor death
- Recipient death
- Preterm pre-labor rupture of the membranes (PPROM)
- Preterm birth, defined as birth prior to 34 weeks’ gestation
- GA at birth (in weeks)
- Interval between laser therapy and delivery
- Maternal bleeding
- Septostomy (either spontaneous or iatrogenic) and chorioamniotic separation

- Placental abruption
- TAPS
- Recurrence of TTTS
- Neonatal morbidity, including respiratory and infectious morbidity and admission to neonatal intensive care unit
- Neurological morbidity including grade III and IV intra-ventricular hemorrhage and grade III and IV periventricular cystic leukomalacia

We also planned to perform sub-group analyses according to GA at treatment and TTTS stage.

Both prospective and retrospective studies reporting data on twin pregnancies complicated by TTTS treated with Solomon vs selective laser coagulation of placental anastomoses were considered suitable for the inclusion. Only full text articles were considered eligible for the inclusion. Case reports, conference abstracts and case series with fewer than five cases were excluded to avoid publication bias.

Two authors (FDA, AK) reviewed all abstracts independently. Agreement regarding potential relevance was reached by consensus. Full text copies of those papers were obtained, and the same two reviewers independently extracted relevant data regarding study characteristics and pregnancy outcome. Inconsistencies were discussed by the reviewers and consensus reached or by discussion with a third author. If more than one study was published for the same cohort with identical endpoints, the report containing the most comprehensive information on the population was included to avoid overlapping populations.

Quality assessment, risk of bias and statistical analysis

Quality assessment of the included studies was performed using the Newcastle-Ottawa Scale (NOS) for case-control studies. According to NOS, each study is judged on three broad

perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of the outcome of interest.[16] Assessment of the selection of a study includes the evaluation of the representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure and the demonstration that the outcome of interest was not present at start of study. Assessment of the comparability of the study includes the evaluation of the comparability of cohorts on the basis of the design or analysis. Finally, the ascertainment of the outcome of interest includes the evaluation of the type of the assessment of the outcome of interest, length and adequacy of follow-up. According to NOS a study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.[16]

We set head-to-head meta-analyses to directly compare, the risk of each of the explored outcomes in pregnancies complicated by TTTS treated compared to those not treated with Solomon technique. In these meta-analyses, we included some cohort studies in which exposed and unexposed group sizes were severely unbalanced, and some studies that reported zero events in one or both of the compared groups. When the events are rare, many of the most commonly used meta-analytical methods can produce biased estimates. When the studies are also substantially imbalanced, the best performing methods are the Mantel-Haenszel odds ratio without zero-cell continuity corrections, logistic regression and an exact method[17-19]. Mantel-Haenszel odds ratios cannot be computed in studies reporting zero events in both groups, the exclusion of which may however cause a relevant loss of information and the potential inflation of the magnitude of the pooled exposure effect.[18] Therefore, to keep all studies into the analyses, the six head-to-head meta-analyses were carried out using individual data random-effect logistic regression, with single study as the cluster unit, and the pooled datasets with individual data were reconstructed using 2X2 tables. Finally, continuous variables were assessed reporting results as pooled mean differences.

Between-study heterogeneity was explored using the I^2 statistic, which represents the percentage of between-study variation that is due to heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity, whereas I^2 values of ≥ 50% indicate a substantial level of heterogeneity. effect model was used when I^2 vales were <50%; conversely a random effect model was used when I^2 values were ≥ 50%.

For each outcome, the total number of publications included in the meta-analyses was <10. We were thus unable to assess publication bias, either graphically, through funnel plots, or formally, through Egger's regression asymmetry test (in such cases, the power is too low to distinguish chance from real asymmetry).[17-19] All analyses were carried out using Stata, version 13.1 (Stata Corp., College Station, TX, 2013).

RESULTS

Study selection and characteristics

Seventy-five articles were identified, 19 were assessed with respect to their eligibility for inclusion and 9 studies were included in the systematic review (Table 1, Figure 1, Table S2)[12,13,20-26]. These 9 studies included (after removing the studies including overlapped cases) 1374 twin pregnancies complicated by TTTS (711 treated with Solomon and 663 with selective laser coagulation of placental anastomoses). Of these studies, one was a RCT, while the remaining studies were observational retrospective series. The results of the quality assessment of the included studies using the NOS scale are presented in Table 2. Most of the included studies showed an overall good score regarding the selection and comparability of study groups, and for ascertainment of the outcome of interest. The main weaknesses of these studies were their retrospective design, small sample size, heterogeneity of the outcomes observed and lack of stratification of the analyses according to the TTTS stage and GA at intervention.

Pregnancy characteristics of twin pregnancies included in the systematic review are reported in Table 3. There was generally no difference in the main maternal and pregnancy characteristics between the twin pregnancies treated using the Solomon technique and those using the selective technique, including maternal mean body mass index (p=0.668), GA at intervention (p= 0.233), number of anastomoses coagulated during the laser surgery (p=0.539), TTTS stage and placental location (p=0.684). Twin pregnancies treated with the Solomon technique had a significantly lower birthweight discordance (pooled MD -2.661, 95% CI -3.978 to -1.344; p=0.001), a higher amount of laser energy used during surgery (pooled Joule MD 2.409, 95% CI 2.0448 to 2.7774, p=0.001) and a lower operation time (MD -2.937, 95% CI -4.569 to -0.225; p=0.031).

Synthesis of the results

Five studies (1072 twin pregnancies) reported the risk of fetal loss in twin pregnancies complicated by TTTS treated using the Solomon technique compared to selective coagulation of placental anastomoses. The risk of fetal loss (pooled OR 0.69, 95% CI 0.50-0.95; p=0.023), neonatal (pooled OR 0.37, 95% CI 0.16-0.84; p=0.018) and perinatal (pooled OR 0.56, 95% CI 0.38-0.83; p=0.004) were significantly lower in pregnancies treated with Solomon technique compared to selective laser coagulation (Table 4). Likewise, pregnancies treated with Solomon technique had a significantly higher chance of survival of at least one twin (pooled OR 1.90, 95% CI 1.1-3.3; p=0.004) and double survivors (pooled OR 1.83, 95% CI 1.2-2.7; p=0.002) and a lower risk of no survivors (pooled OR 0.55, 95% CI 0.31-0.95; p=0.004) compared to those treated with selective photocoagulation (Figure 2). The risk of recipient death was also significantly lower in twin pregnancies complicated by TTTS which were treated using the Solomon technique (pooled OR 0.42, 95% CI 0.22-0.80; p=0.009), while there was no significant difference in the risk of donor death between the two groups (p=0.187).

When exploring maternal outcomes, there was no significant difference in the risk of PPROM (p=0.735), PPROM within 10 days from laser (P=0.982), PTB (p=0.207), maternal bleeding (p=0.322), septostomy or chorioamniotic separation (p=0.670), and chorioamnionitis (p=0.135) between the two groups, while the risk of placental abruption was significantly higher in the twin pregnancies treated with Solomon technique (pooled OR 2.93, 95% CI 1.6-5.5; p=0.001). Pregnancies undergoing Solomon technique delivered at significantly earlier GA compared to those with selective laser (pooled MD -0.625 weeks, 95% CI -0.90 to -0.35, p<0.001), while there was no significant difference in the interval between laser surgery and delivery (pooled MD -0.04, 95% CI -0.191 to 0.109, p=0.589).

Recurrence of TTTS was significantly lower in the pregnancies undergoing Solomon technique (pooled OR 0.43, 95% CI 0.24-0.91; p<0.001), while there was no significant difference in the risk of TAPS between the two groups (p=0.792).

Assessment of perinatal morbidity was affected by the very small number of cases included and even smaller number of events which precluded a comprehensive pooled analysis. Overall, there was no significant difference in the overall risk of neonatal morbidity (p=0.382) and neurological morbidity (p=0.247) between the two groups.

A comprehensive sub-group analysis according to TTTS stage and GA at intervention could not be performed because none of the included study reported this information.

DISCUSSION

Main findings

The findings from this systematic view showed that twin pregnancies complicated by TTTS and treated with Solomon technique have a significantly higher survival rate compared to those treated with selective laser coagulation of placental anastomoses. The risk of placental abruption was significantly higher in the pregnancies treated with the Solomon technique while there was no significant difference in the incidence of PTB, PPROM or chorioamnionitis between the two groups. Finally, there was no significant difference in the risk of overall morbidity and neurological morbidity between the two groups.

Strengths and limitations

Thorough literature search, multitude of outcomes explored and assessment of potential confounders in affecting maternal and perinatal outcomes are the main strengths of the present review. The small number of cases in some of the included studies, their retrospective non-randomized design, lack of standardized criteria for the surveillance after the procedure and lack of stratification according to GA at intervention and TTTS staging represent the main weakness of this systematic review.

Comparison with other published evidence

A previous systematic review comparing the outcome of twin pregnancies complicated by TTTS treated with the Solomon technique compared to selective coagulation included three studies and reported a statistically significant reduction in risk of recurrent TTTS, but not TAPS or perinatal survival between the two techniques[27]. In the present systematic review, we added a larger number of studies as well as observed outcomes.

Clinical and research implications

The mainstay of the laser treatment for TTTS is the complete photocoagulation of all placental anastomoses. TTTS is a hemodynamic condition characterized by unbalanced blood flow

through placental anastomoses and the presence of residual placental anastomoses may be associated with persistence of TTTS, post-Laser TAPS, need for re-intervention, postnatal hemoglobin difference but not mortality[28]. The Solomon technique was developed to reduce the risk of leaving residual anastomoses after laser surgery. A secondary analysis of the Solomon trial exploring the risk of persistent residual anastomoses in pregnancies treated with Solomon technique compared to selective ablation of placental anastomoses has reported that the proportion of placentas with residual anastomoses in the Solomon group and Standard group was 19% and 34%, respectively. Therefore, confirming the beneficial effect of Solomon technique in reducing the rate of residual anastomoses[29].

Residual anastomoses might be responsible of recurrent TTTS and TAPS. Furthermore, placental anastomoses can affect the outcome of MC twins complicated by selective fetal growth restriction[30-38]. In the present systematic review, the risk of recurrent TTTS, but not that of TAPS, was significantly lower in the pregnancies undergoing Solomon technique compared to selective ablation of placental anastomoses. The apparently lack of significant association between Solomon technique and lower risk of TAPS is surprising and could be explained by a number of theories. Firstly, although the Solomon Trial has reported a lower risk of a composite outcome including TAPS, recurrence of TTTS, perinatal mortality, or severe neonatal morbidity but was not powered to detect differences in the individual components of the primary outcome, although the authors reported a significant reduction of TAPS in pregnancies treated with Solomon technique. Secondly, the lack of association between the Solomon technique and TAPS might be the result of different monitoring protocols undertaken after laser therapy. More importantly, the definition of TAPS has been recently revised and this might have contributed to the different rates of post-laser TAPS reported in the different series. Thirdly, neither the Solomon trial nor the observational studies included in our systematic review considered the factors potentially affecting the rate of residual anastomoses such as their diameter, location (central vs peripheral) or placental position (anterior vs posterior). Lastly, TAPS is a relatively rare condition and the small number of cases included

in the present systematic review are likely to make this review underpowered for this outcome. In the present systematic review, the cumulative incidence of TAPS after laser surgery was about 4.4% compared to 9% observed in the RCT by Slaghekke et al. and this may further explain the lack of association between Solomon technique and reduced risk of post-laser TAPS.

Since the initial reports, concerns have been raised on the possible association between Solomon technique and increased risk of placental abruption, preterm birth and PPROM. Solomon technique is associated with greater amount of laser energy used during surgery which may lead to tissue damage, which may explain the higher risk of placental abruption observed in the present review. However, establishing an association between laser technique and placental abruption is not straightforward as other factors may potentially explain the higher incidence of abruption in these women. In the present systematic review, the total amount of laser energy was higher in pregnancies treated using the Solomon technique compared to selective coagulation. Likewise, we reported a significantly higher risk of placental abruption and lower GA at delivery in pregnancies undergoing the Solomon technique. Early gestational age at PPROM, polyhydramnios and fetal growth restriction are commonly found in association with TTTS and may also account for a higher risk of placental abruption observed in women undergoing laser therapy using the Solomon technique, which may occur even months after laser therapy. Akkerrman et al. reported that higher gestational age at intervention, increased amount of laser energy and visual tissue damage were associated with a higher risk of PPROM before 32 weeks of gestation and early gestational age at birth[39].

This risk should be communicated to the parents during pre-surgical counselling, although it should be stressed that such technical approach is associated with improved survival, which is the main purpose of the treatment. Further modifications of the original Solomon technique

should be aimed at avoiding unnecessary damage of placental tissue, thus reducing the risk of placental related complications.

Conclusions

Monochorionic twin pregnancies complicated by TTTS undergoing laser treatment using the Solomon technique had a higher survival rate and lower rate of recurrent TTTS, but an increased risk of placental abruption compared to those treated with selective coagulation of placental anastomoses. Future studies are needed to elucidate whether modifications to the original Solomon technique could reduce the risk of placental abruption.

REFERENCES

1. Hayes EJ. Practice bulletin no. 169: multifetal gestations: twin, triplet, and higher-order multifetal pregnancies. *Obstet Gynecol* 2016; **128**: e131–e146.
2. Society for Maternal-Fetal Medicine, Simpson LL. Twin-twin transfusion syndrome. *Am J Obstet* Gynecol 2013; **208**: 3–18.
3. D'Antonio F, Thilaganathan B, Dias T, Khalil A; Southwest Thames Obstetric Research Collaborative (STORK). Influence of chorionicity and gestational age at single fetal loss on risk of preterm birth in twin pregnancy: analysis of STORK multiple pregnancy cohort. *Ultrasound Obstet Gynecol* 2017; **50**: 723–727.
4. D'Antonio F, Khalil A, Dias T, Thilaganathan B; Southwest Thames Obstetric Research Collaborative (STORK). Early fetal loss in monochorionic and dichorionic twin pregnancies: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort. *Ultrasound Obstet Gynecol* 2013; **41**: 632–6.
5. Murgano D, Khalil A, Prefumo F, Mieghem TV, Rizzo G, Heyborne KD, Melchiorre K, Peeters S, Lewi L, Familiari A, Lopriore E, Oepkes D, Murata M, Anselem O, Buca D, Liberati M, Hack K, Nappi L, Baxi LV, Scambia G, Acharya G, D'antonio F. Outcome of twin-to-twin transfusion syndrome in monochorionic monoamniotic twin pregnancy: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2020; **55**: 310–317.
6. D'Antonio F, Khalil A, Dias T, Thilaganathan B; Southwest Thames Obstetric Research Collaborative. Crown-rump length discordance and adverse perinatal outcome in twins: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort. *Ultrasound Obstet Gynecol* 2013; **41**: 621–626.
7. Senat MV, Deprest J, Boulvain M, Paupe A, Winer N, Ville Y. Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. *N Engl J Med* 2004; **351**: 136–144.
8. Ville Y, Hyett J, Hecher K, Nicolaides K. Preliminary experience with endoscopic laser surgery for severe twin–twin transfusion syndrome. *N Engl J Med* 1995; **332**: 224–227.
9. Robyr R, Lewi L, Salomon LJ, Yamamoto M, Bernard JP, Deprest J, Ville Y. Prevalence

and management of late fetal complications following successful selective laser coagulation of chorionic plate anastomoses in twin-to-twin transfusion syndrome. *Am J Obstet Gynecol* 2006; **194**: 796–803

10. Quintero RA, Ishii K, Chmait RH, Bornick PW, Allen MH, Kontopoulos EV. Sequential selective laser photocoagulation of communicating vessels in twin–twin transfusion syndrome. *J Matern Fetal Neonatal Med* 2007; **20**: 763–768.
11. Lopriore E, Slaghekke F, Middeldorp JM, Klumper FJ, Oepkes D, Vandenbussche FP. Residual anastomoses in twin-to-twin transfusion syndrome treated with selective fetoscopic laser surgery: localization, size, and consequences. *Am J Obstet Gynecol* 2009; **201**: 66.e1–4
12. Ruano R, Rodo C, Peiro JL, Shamshirsaz AA, Haeri S, Nomura ML, Salustiano EM, de Andrade KK, Sangi-Haghpeykar H, Carreras E, Belfort MA. Fetoscopic laser ablation of placental anastomoses in twin–twin transfusion syndrome using 'Solomon technique'. *Ultrasound Obstet Gynecol* 2013; **42**: 434–439.
13. Slaghekke F, Lopriore E, Lewi L, Middeldorp JM, van Zwet EW, Weingertner AS, Klumper FJ, DeKoninck P, Devlieger R, Kilby MD, Rustico MA, Deprest J, Favre R, Oepkes D. Fetoscopic laser coagulation of the vascular equator versus selective coagulation for twin-to-twin transfusion syndrome: an open-label randomised controlled trial. *Lancet* 2014; **383**: 2144–2151.
14. Henderson LK, Craig JC, Willis NS, Tovey D, Webster AC. How to write a Cochrane systematic review. *Nephrology (Carlton)* 2010; **15**: 617-624.
15. NHS Centre for Reviews and Dissemination. Systematic reviews: CRD's guidance for undertaking reviews in health care. University of York: York (UK), 2009. Available at: https://www.york.ac.uk/media/crd/Systematic_Reviews.pdf. Retrieved December 3, 2016.
16. Newcastle-Ottawa Scale for assessing the quality of nonrandomised studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
17. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal

for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. J*AMA* 2000; **283**: 2008–2012.

18. Hunter JP, Saratzis A, Sutton AJ, Boucher RH, Sayers RD, Bown MJ. In meta-analyses of proportion studies, funnel plots were found to be an inaccurate method of assessing publication bias. *J Clin Epidemiol* 2014; **67**: 897–903.
19. Manzoli L, De Vito C, Salanti G, D'Addario M, Villari P, Ioannidis JP. Meta-analysis of the immunogenicity and tolerability of pandemic influenza A 2009 (H1N1) vaccines. *PLoS One* 2011; **6**: e24384.
20. Fichera A, Azzaretto VV, Fratelli N, Mancino S, Marella D, Negri B, Valcamonico A, Zanardini C, Frusca T, Sartori E, Prefumo F. Fetoscopic laser ablation therapy in monochorionic diamniotic twin pregnancies with twin-to-twin transfusion syndrome treated at a single centre over 10 years: a retrospective study. *J Perinat Med* 2021; **50**: 34–41.
21. Kanazawa S, Ozawa K, Muromoto J, Sugibayashi R, Wada Y, Wada S, Ito Y, Sago H. Risk Profiling of the Solomon Technique versus Selective Technique of Fetoscopic Laser Surgery for Twin-Twin Transfusion Syndrome. *Twin Res Hum Genet* 2021; **24**: 42–48.
22. Knijnenburg PJC, Lopriore E, Ge Y, Scholl IM, van Klink JMM, Haak MC, Middeldorp JM, Klumper FJCM, Oepkes D, Sun L, Slaghekke F. Placental Abruption after Fetoscopic Laser Surgery in Twin-Twin Transfusion Syndrome: The Role of the Solomon Technique. *Fetal Diagn Ther* 2021; **48**: 660–666.
23. Kim R, Lee MY, Won HS, Kim JM, Lee YJ, Jeong BD, Kim HJ. Perinatal outcomes and factors affecting the survival rate of fetuses with twin-to-twin transfusion syndrome treated with fetoscopic laser coagulation: a single-center seven-year experience. *J Matern Fetal Neonatal Med* 2021: 1–12.
24. Lanna MM, Faiola S, Consonni D, Rustico MA. Increased risk of placental abruption after solomon laser treatment of twin-twin transfusion syndrome. *Placenta* 2017; **53**: 54–56.
25. van Klink JM, Slaghekke F, Balestriero MA, Scelsa B, Introvini P, Rustico M, Faiola S, Rijken M, Koopman HM, Middeldorp JM, Oepkes D, Lopriore E. Neurodevelopmental

outcome at 2 years in twin-twin transfusion syndrome survivors randomized for the Solomon trial. *Am J Obstet Gynecol* 2016; **214**: 113.e1–7.

26. Baschat AA, Barber J, Pedersen N, Turan OM, Harman CR. Outcome after fetoscopic selective laser ablation of placental anastomoses vs equatorial laser dichorionization for the treatment of twin-to-twin transfusion syndrome. *Am J Obstet Gynecol* 2013; **209**: 234.e1–8.
27. Dhillon RK, Hillman SC, Pounds R, Morris RK, Kilby MD. Comparison of Solomon technique with selective laser ablation for twin-twin transfusion syndrome: a systematic review. *Ultrasound Obstet Gynecol* 2015; **46**: 526–533.
28. Di Mascio D, Khalil A, D'Amico A, Buca D, Benedetti Panici P, Flacco ME, Manzoli L, Liberati M, Nappi L, Berghella V, D'Antonio F. Outcome of twin-twin transfusion syndrome according to Quintero stage of disease: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2020; **56**: 811–820.
29. Slaghekke F, Lewi L, Middeldorp JM, Weingertner AS, Klumper FJ, Dekoninck P, Devlieger R, Lanna MM, Deprest J, Favre R, Oepkes D, Lopriore E. Residual anastomoses in twin-twin transfusion syndrome after laser: the Solomon randomized trial. *Am J Obstet Gynecol* 2014; **211**: 285.e1–7.
30. Buca D, Pagani G, Rizzo G, Familiari A, Flacco ME, Manzoli L, Liberati M, Fanfani F, Scambia G, D'Antonio F. Outcome in monochorionic twin pregnancies with selective intrauterine growth restriction according to the umbilical artery Doppler pattern of the smaller twin: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2017; **50**: 559–568.
31. Leombroni M, Liberati M, Fanfani F, Pagani G, Familiari A, Buca D, Manzoli L, Scambia G, Rizzo G, D'Antonio F. Diagnostic accuracy of ultrasound in detecting birthweight discordance in twin pregnancies: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2017; **50**: 442–450.
32. D'Antonio F, Odibo A, Prefumo F, Khalil A, Buca D, Flacco M, Liberati M, Manzoli L, Acharya G. Weight discordance and perinatal mortality in twin pregnancies: a systematic

review and meta-analysis. *Ultrasound Obstet Gynecol* 2018; **52**: 11–23.

33. D'Antonio F, Odibo A, Berghella V, Khalil A, Kack K, Saccone G, Prefumo F, Buca D, Liberati M, Pagani G, Acharya G. Systematic review and meta-analyses of monoamniotic twin pregnancies: Perinatal mortality, timing of delivery and prenatal management. *Ultrasound Obstet Gynecol* 2019; **53**: 166–174.
34. Di Mascio D, Acharya G, Khalil A, Odibo A, Prefumo F, Liberati M, Buca D, Manzoli L, Flacco ME, Brunelli R, Benedetti Panici P, D'Antonio F. Birthweight discordance and neonatal morbidity in twin pregnancies: a systematic review and meta-analysis. *Acta Obstet Gynecol Scand* 2019; **98**: 1245–1257.
35. Saccone G, Khalil A, Thilaganathan B, Glinianaia SV, Berghella V, D'Antonio F; MONOMONO; NorSTAMP; STORK research collaboratives. Weight discordance and perinatal mortality in monoamniotic twin pregnancies: analysis of the MONOMONO, NorSTAMP and STORK multiple pregnancy cohorts. *Ultrasound Obstet Gynecol* 2020; 55: 332–338.
36. MONOMONO Working Group. Inpatient vs outpatient management and timing of delivery of uncomplicated monochorionic monoamniotic twin pregnancy: the MONOMONO study. *Ultrasound Obstet Gynecol* 2019; **53**: 175–183.
37. Pagani G, D'Antonio F, Khalil A, Papageorghiou A, Bhide A, Thilaganathan B. Intra-fetal laser treatment for twin reversed arterial perfusion sequence: cohort study and meta-analysis. *Ultrasound Obstet Gynecol* 2013; **42**: 6–14.
38. Lenclen R, Ciarlo G, Paupe A, Bussieres L, Ville Y. Neurodevelopmental outcome at 2 years in children born preterm treated by amnioreduction or fetoscopic laser surgery for twin-to-twin transfusion syndrome: comparison with dichorionic twins. *Am J Obstet Gynecol* 2009; **201**: 291.e1–5.
39. Akkermans J, de Vries SM, Zhao D, Peeters SHP, Klumper FJ, Middeldorp JM, Oepkes D, Slaghekke F, Lopriore E. What is the impact of placental tissue damage after laser surgery for twin-twin transfusion syndrome? A secondary analysis of the Solomon trial. *Placenta* 2017; **52**: 71–76.

D'Antonio Francesco (Orcid ID: 0000-0002-7546-8025)
Khalil Asma (Orcid ID: 0000-0003-2802-7670)

FIGURE LEGENDS

Figure 1. Systematic review flowchart.

Figure 2. Pooled odds ratios of perinatal loss (2a) and survival of at least one twin (2b), placental abruption (2c) and TTTS recurrence (2d) in monochorionic twin pregnancies complicated by TTTS undergoing placental dichorionization (Solomon technique) compared to selective Laser coagulation of placental anastomoses.

Table 1. General characteristics of the studies included in the systematic review.

First author	Year	Country	Study design	Study period	Primary outcome	Stratification according to TTTS Stage or GA at laser	Pregnancies (n)
Fichera[20]	2022	Italy	Retrospective (single centre)	2008-2018	Perinatal outcomes	No	133
Kanazawa[21]	2021	Japan	Retrospective (single centre)	2010-2017	Pregnancy and perinatal outcomes	No	395
Knijnenburg[22]	2021	The Netherlands-China	Retrospective (multicentre)	2002-2022	Placental abruption	No	730
Kim[23]	2021	Korea	Retrospective (single centre)	2011-2018	Perinatal outcomes	No	173
Lanna[24]	2017	Italy	Retrospective (single centre)	2004-2015	Placental abruption	No	373
Van Klink[25]	2016	The Netherlands-Italy	Prospective	2008-2012	Survival without long-term neurodevelopmental impairment at age 2 years	No	216
Slaghekke[13]	2014	The Netherlands-Italy-France-United Kingdom	Multicentre RCT	2008-2012	Composite of incidence of twin anaemia polycythaemia sequence, recurrence of twin-to-twin transfusion syndrome, perinatal mortality, or severe neonatal morbidity	No	272
Ruano[12]	2013	United States-Brazil-Spain	Retrospective (multicentre)	2010-2012	Pregnancy and perinatal outcomes	No	102
Baschat[26]	2013	United States-Brazil-Spain	Retrospective (single centre)	2005-2011	Preoperative, procedural and birth outcomes	No	147

GA: gestational age

Table 2. Quality assessment of the included studies according to Newcastle-Ottawa Scale (NOS); a study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Author	Year	Selection	Comparability	Outcome
Fichera[20]	2022	★★★	★	★★
Kanazawa[21]	2021	★★★	★	★★
Knijnenburg[22]	2021	★★	★★	★★
Kim[23]	2021	★★★	★	★★
Lanna[24]	2017	★★★	★	★★
Van Klink[25]	2016	★★	★	★★
Slaghekke[13]	2014	★★	★★	★★
Ruano[12]	2013	★★	★	★★
Baschat[26]	2013	★★	★	★★

Table 3. General characteristics of the study population.

Characteristics	Studies	References	Mean and SD (cases)	Pooled MD (95% CI)	SE	P-values
Maternal body mass index (kg/m^2)	3	20,21,26	(283) 25.9±4.7 vs 23.8± 4.9 (392)	-0.091 (-0.505 to 0.324)	0.211	0.668
Gestational age at intervention (weeks)	7	12,13 20,21,23,24,25,26	(562) 20.5±2.5 vs 20.5± 2.5 (660)	-0.070 (-0.186 to 0.045)	0.059	0.233
Birthweight discordance (%)	3	12,21,26	(236) 21.0 ±5.9 vs 21.5± 11.6 (307)	-2.661 (-3.978 to -1.344)	0.672	0.001
Operation time (min)	6	13,20,21,22,23,26	(586) 41.1± 16.6 vs 42.7± 18.9 (584)	-2.937 (-4.569 to -0.225)	1.108	0.031
Number of anastomoses	3	13,23,26	(192) 14.05±8.7 vs 12.81± 6.1 (128)	0.497 (-1.090 to 2.083)	0.809	0.539
Laser Energy (J)	4	21,22,13,26	(381) 8622.3±4449.4 vs 6761.3±3799.3 (433)	2.409 (2.0448 to 2.7774)	185.9	0.001

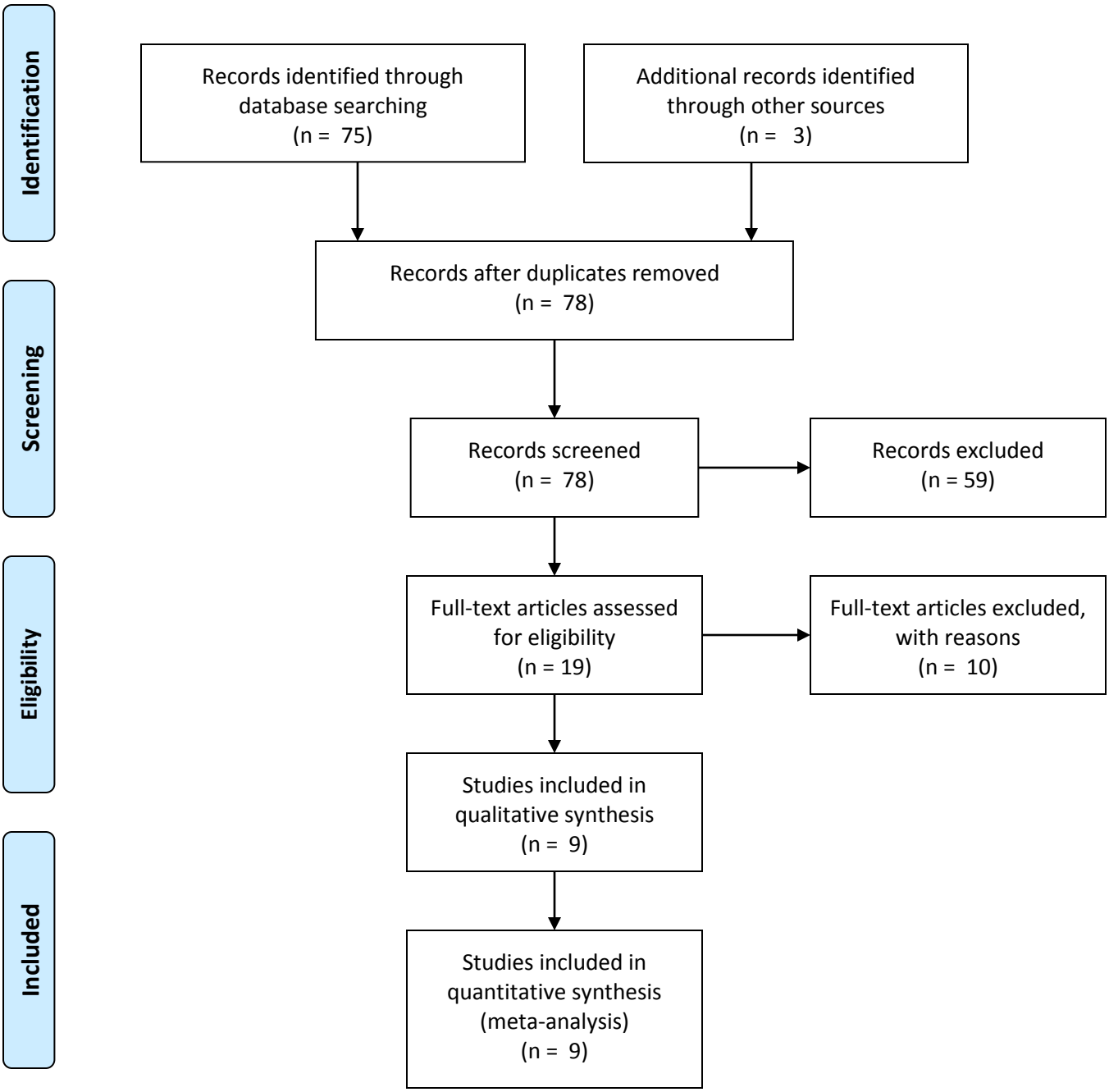
Characteristics	Studies	References	Cases (n/N vs n/N)	I^2 (%)	Pooled OR (95% CI)	P-values
Anterior placenta	6	12,13,20,21,23,26	247/567 vs 292/600	0	0.97 (0.77-1.2)	0.864
TTTS stage I	6	12,13, 20,21,23,26	97/567 vs 92/660	0	1.21 (0.88-1.7)	0.280
TTTS stage II	6	12,13, 20,21,23,26	159/567 vs 183/660	71.2	1.11 (0.67-1.8)	0.682
TTTS stage III	6	12,13, 20,21,23,26	274/567 vs 340/660	77.9	0.85 (0.50-1.4)	0.558
TTTS stage IV	6	12,13, 20,21,23,26	37/567 vs 40/660	48.7	0.87 (0.41-1.9)	0.725

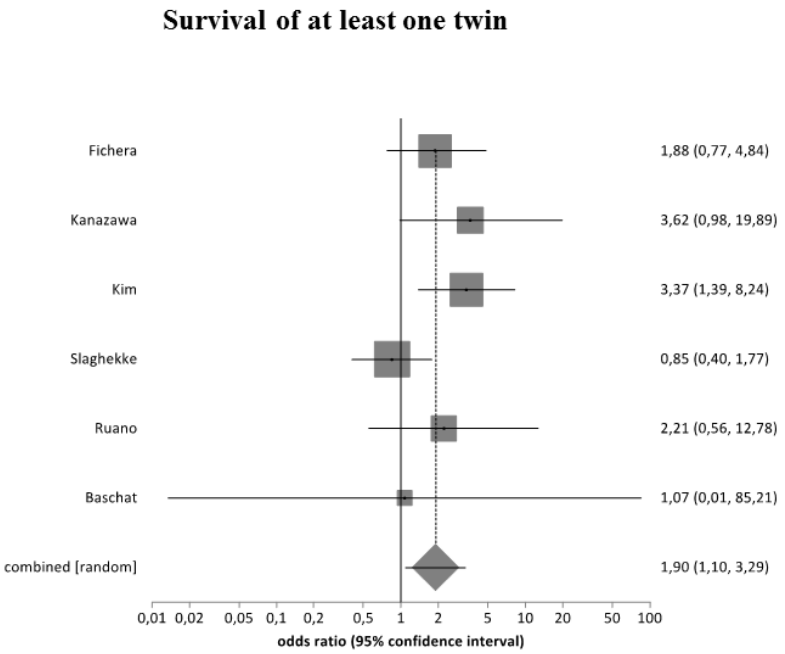
Table 4. Pooled or (95% CI) for the different outcomes explored in the present systematic review in twin pregnancies complicated by TTTS undergoing placental dichorionization (Solomon technique) compared to selective coagulation of placental anastomoses.

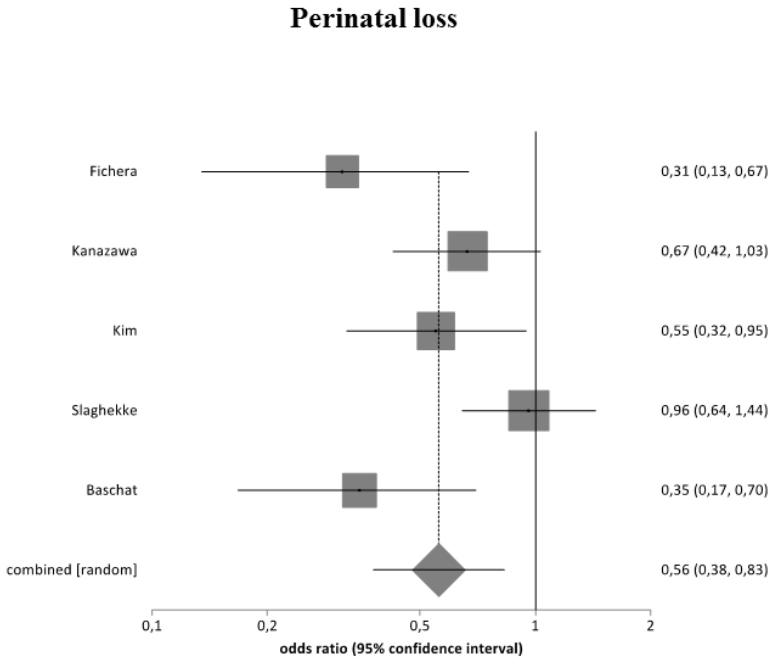
Study outcomes	Studies	References	Cases (n/N vs n/N)	I^2 (%)	Pooled OR (95% CI)	P-values
Mortality						
Fetal loss	5	13,20,21,23,26	160/1072 vs 223/1168	42.8	0.69 (0.50-0.95)	0.023
Neonatal death	5	13,20,21,23,26	21/1072 vs 52/1168	44.6	0.37 (0.16-0.84)	0.018
Perinatal loss	5	13,20,21,23,26	181/1072 vs 275/1168	65.8	0.56 (0.38-0.83)	0.004
Survival of at least one twin	6	12,13,20,21,23,26	511/562 vs 556/660	36.3	1.90 (1.10-3.29)	0.004
Survival of both twins	6	12,13,20,21,23,26	404/562 vs 404/660	50.2	1.83 (1.2-2.7)	0.002
No survivors	6	12,13,20,21,23,26	91/562 vs 121/660	37.6	0.55 (0.31-0.95)	0.004
Donor death	2	20,21	35/207 vs 84/321	71.3	0.49 (0.17-1.4)	0.187
Recipient death	2	20,21	13/207 vs 49/321	0	0.42 (0.22-0.80)	0.009
Pregnancy complications						
Preterm pre-labor rupture of the membranes (PPROM)	4	20,21,22,26	175/724 vs 128/685	86.9	1.20 (0.4-3.4)	0.735
PPROM within 10 days form laser	2	20,23	8/155 vs 8/151	19.4	0.98 (0.22-4.2)	0.982
Preterm birth	2	21,26	84/244 vs 128/303	0	0.77 (0.53-1.1)	0.207
Maternal bleeding	4	13,20,23,26	24/368 vs 34/362	74.8	0.50 (0.13-1.9)	0.322
Septostomy or chorioamniotic separation	5	12,20,22,23,26,	91/698 vs 84/592	27.1	0.81 (0.61-1.1)	0.670
Chorioamnionitis	3	13,23,26	4/329 vs 7/268	4.9	0.36 (0.10-1.3)	0.135
Placental abruption	3	21,22,26	39/685 vs 14/592	0	2.93 (1.6-5.5)	0.001

Twin anemia polycythemia sequence (TAPS)	6	12,13,20,21,23,26	20/562 vs 34/660	63.9	0.84 (0.23-3.1)	0.792
Recurrence of TTTS	6	12,13,20,21,23,26	14/562 vs 38/660	0	0.43 (0.24-0.91)	<0.001
	Postnatal outcome					
Neonatal morbidity	2	13,20	30/282 vs 49/339	27.4	0.77 (0.43-1.39)	0.382
Neurological morbidity	3	13,20,23	19/357 vs 44/369	91.9	0.17 (0.13-3.3)	0.2466

PRISMA 2009 Flow Diagram







Placental abruption