Received: 26 October 2023 | Revised: 8 January 2024 | Accepted: 31 January 2024

DOI: 10.1111/aogs.14806

AOGS Acta Obstetricia et Gynecologica Scandinavica

SYSTEMATIC REVIEW

Perinatal outcomes following fetoscopic laser surgery for early twin-to-twin transfusion syndrome: Systematic review and meta-analysis

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Abstract

Introduction: Our objective was to investigate outcomes in twin-to-twin transfusion syndrome (TTTS) treated with fetoscopic laser surgery (FLS) at <18 weeks vs ≥18 weeks, and to conduct subgroup analysis of TTTS with FLS at <16 weeks vs 16–18 weeks.

Material and methods: PubMed, Scopus and Web of Science were searched systematically from inception until May 2023. Primary outcome was survival, and secondary outcomes included preterm premature rupture of membranes (PPROM), preterm birth and gestational age (GA) at delivery.

Results: Nine studies encompassing 1691 TTTS pregnancies were included. TTTS stage III was significantly more common in TTTS pregnancies treated with FLS at <18 weeks (odds ratio [OR] 2.84, 95% confidence interval [CI] 1.24–6.54), and procedure duration was shorter at <18 weeks (MD −5.27 minutes, 95% CI −9.19 to −1.34). GA at delivery was significantly earlier in TTTS pregnancies treated with FLS at <18 weeks (MD −3.12 weeks, 95% CI −6.11 to −0.13). There were no significant differences in outcomes, including PPROM, PPROM at <7 days post-FLS, preterm birth at <28 and <32 weeks, delivery at <7 days post-FLS, and survival outcomes, including fetal demise, live birth and neonatal survival. Similarly, TTTS stage III was more common in TTTS with FLS at <16 weeks than at 16–18 weeks (OR 2.95, 95% CI 1.62–5.35), with no significant differences in the aforementioned outcomes.

Conclusions: In early TTTS treated with FLS, outcomes were comparable between those treated at <18 weeks compared with ≥18 weeks except for GA at delivery, which was 3 weeks earlier. In the subset treated at <16 weeks vs 16–18 weeks, the procedure was feasible without an increased risk of very early preterm birth or perinatal mortality.

KEYWORDS
fetoscopy, laser, meta-analysis, monochorionic, systematic review, twin, twin-to-twin transfusion

Abbreviations: CI, confidence interval; FLS, fetoscopic laser surgery; GA, gestational age; MD, mean difference; OR, odds ratio; PPROM, preterm premature rupture of membranes; PTB, preterm birth; RCT, randomized controlled trial; TTTS, twin-to-twin transfusion syndrome.

1 | INTRODUCTION

Twin-to-twin transfusion syndrome (TTTS) is a complication in about 8%–15% of monochorionic/diamniotic twin pregnancies,[1,2] with a prevalence of 1–3 per 10000 births.[3] The underlying etiology of TTTS is the imbalance of blood flow across placental intertwin vascular anastomoses, leading to volume depletion and overload in the donor and recipient twins, respectively.[4] TTTS is a severe complication; if left untreated, its mortality rate exceeds 90%, and fetuses who survive, struggle with a wide range of cardiovascular and neurodevelopmental complications.[5,6]

The Quintero system[7] for staging TTTS based on sonographic findings[8] remains the most useful tool for identifying cases most likely to benefit from treatment.[9] Fetoscopic laser surgery (FLS) is the management of choice, with more favorable survival and neurological outcome than serial amnioreduction for TTTS stages II–IV between 16 and 26 weeks' gestational age (GA).[10,11] The Eurofoetus trial group recommends this strict gestational age (GA) cutoff,[10] and it has been hypothesized that FLS is more challenging in early TTTS due to the absence of chorioamniotic fusion.[12,13] However, given the advances in technique and material, surgical experience, few centers offer and perform FLS at <16 weeks.[14–18]

A systematic review from 2020 showed that twin pregnancies affected by early twin-to-twin transfusion syndrome are at substantial risk of perinatal mortality and morbidity; however, data at that time came from very small case series with no head-to-head comparisons.[19] Few larger studies have been published since that last review providing data on outcomes for early TTTS.[20–23] Knowing that there is still no consensus on the optimal management for early TTTS, we aimed to provide an updated systematic review and meta-analysis of pregnancy characteristics and outcomes in TTTS with FLS at <18 weeks vs ≥18 weeks and to perform a subgroup analysis for those at <16 weeks vs 16–18 weeks.

Key message

Although gestational age at delivery was 3 weeks earlier in TTTS with fetoscopic laser surgery at <18 weeks, there was no difference in outcomes including very early preterm birth, premature rupture of membranes, and survival with similar findings in the subset that underwent laser surgery at <16 weeks.

2 | MATERIAL AND METHODS

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines.[24] The study protocol for this systematic review was registered in the PROSPERO international prospective register of systematic reviews (Registration number CRD42023441058).

2.1 | Search strategy

PubMed, Web of Science and Scopus were searched from inception to May 2023. Initially selected studies were reviewed for eligibility by two independent authors (MB and PS), and conflicts were resolved by consulting a third investigator (HJM). The search was conducted using combinations of the relevant medical subject heading (MeSH) terms, keywords and word variants for ("fetofetal transfusion") AND ("outcome" OR "sequelae" OR "morbidity"). References of relevant articles were manually reviewed and eligible studies were added to results from an electronic literature search. Search strategies are reported in Table S1.

2.2 | Selection of studies

Studies generated from the search process were transferred into Rayyan, an automated web application designed to screen the papers for systematic reviews.[25] Duplications were removed through function in Rayyan, following which a manual check for duplicates was also performed. The studies were selected in two phases. First, titles and abstracts of the articles were screened independently by two reviewers (MB and PS). Full-text copies of the selected articles were assessed independently for their eligibility by the same two reviewers according to the inclusion and exclusion criteria described below. Disagreements between reviewers were resolved by discussion or by a third reviewer (HM). In the case of overlapping studies, only the largest and most complete dataset was included.

2.3 | Inclusion and exclusion criteria

Using the PICO (Patient-Intervention-Comparison-Outcome) framework, the following eligibility criteria were determined to include all relevant original articles: (P) Population: pregnancies with TTTS; (I) Intervention/indicator: FLS; (C) Comparison: comparison of two groups [TTTS with FLS at <18 weeks vs ≥18 weeks and TTTS with FLS at <16 weeks vs 16–18 weeks]; (O) Outcome: survival, preterm premature rupture of membranes (PPROM), preterm birth (PTB) and GA at delivery.

Inclusion criteria were randomized control trials (RCT), cohort, case control or case series studies evaluating MC twin pregnancies complicated with TTTS and requiring FLS and providing data on these with treatment at <18 weeks vs ≥18 weeks. Exclusion criteria consisted of narrative review articles, systematic reviews and conference abstracts.

2.4 | Data extraction

The following variables were extracted from the full-text of included records: year of publication, country of the study, institution name, maternal characteristics such as age, parity and body mass index (BMI), obstetrical characteristics such as TTTS stage, placental position, cervical length, PPROM, PTB, GA at delivery, FLS-to-delivery interval, and survival/mortality outcomes including single/double fetal demise, donor/recipient demise, single/double survival at birth, and single/double neonatal survival.

2.5 | Quality assessment

The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of included cohort or case–control studies and the risk of bias. NOS comprises “participant selection”, “comparability of study groups” and “assessment of outcome or exposure”. A score >7 is considered to be high quality.[26]

2.6 | Data synthesis and statistical analysis

R (R Foundation for Statistical Computing, Vienna, Austria) and RStudio (RStudio, Inc., Boston, MA, USA) were used for cleaning the data, statistical analysis and creating the forest and funnel plots. Variables reported in median with range or interquartile range were converted to mean and standard deviation using the Wan formula.[27] Pooled effect sizes were presented using mean difference (MD) or odds ratio (OR), using the Mantel–Haenszel test, with 95% confidence interval (CI) for continuous and categorical variables, respectively. Only variables that were reported in at least two studies were analyzed. *I*-square tests (I^2) were used to examine heterogeneity across the included studies; $I^2 \geq 50\%$ and $P < 0.05$ indicate heterogeneity; $I^2 > 75\%$ represents considerable heterogenicity. A random-effects model was used owing to the anticipated heterogeneity of included studies. Leave-one-out analysis was performed for significant variables to demonstrate the impact of each study on the pooled results by removing each of them one at a time. Potential publication bias was assessed using Begg's correlation test. A *P*-value <0.05 was considered statistically significant.

3 | RESULTS

3.1 | Search strategy and study characteristics

As shown in the PRISMA flow chart (Figure 1), a total of 1361 articles were retrieved from three databases. Of those articles, 654 were excluded for duplication. The remaining 707 studies were screened for eligibility. Title and abstract screening resulted in 61 potentially eligible studies. After a full-text assessment was performed, nine studies encompassing 1691 TTTS pregnancies were included.[20,21,23,28–33] Study characteristics are presented in Table 1. Included studies were published between 2002 and 2023. Two studies were conducted in France,[23,31] one each in the USA,[21] Canada,[32] Malaysia,[20] Chile,[29] Spain,[30] Germany[28] and the UK.[33] Five studies were retrospective cohorts and four were prospective cohorts. Inclusion, exclusion criteria and outcomes included in the analysis per each study are outlined in Table 1.

3.2 | Obstetrical and survival outcomes in TTTS pregnancies undergoing FLS at <18 weeks vs ≥18 weeks

Twin-to-twin transfusion syndrome stage III was significantly more common in TTTS pregnancies treated with FLS at <18 weeks than at ≥18 weeks (OR 2.84, 95% CI 1.24–6.54), and FLS procedure duration was shorter at <18 weeks than at >18 weeks (MD −5.27 minutes, 95% CI −9.19 to −1.34) (Table 2). GA at delivery was significantly earlier in TTTS pregnancies treated with FLS at <18 weeks vs ≥18 weeks (MD −3.12 weeks, 95% CI −6.11 to −0.13). There were no significant differences in prenatal factors, including maternal age, nulliparity, anterior placentation, cervical length and cerclage placement, or in other obstetrical outcomes, including PPROM, PPROM at <7 days post-FLS, PTB at <28 weeks, PTB at <32 weeks, delivery at <7 days post-FLS, or in survival outcomes including single/double fetal demise, donor or recipient demise, single/double live birth, and single/double neonatal survival (Table 2).

3.3 | Obstetric and survival outcomes in TTTS pregnancies undergoing FLS at <16 weeks vs 16–18 weeks

Stage III TTTS appeared to be more common at <16 weeks than at 16–18 weeks (OR 2.95, 95% CI 1.62–5.35) (Table 3). There were no significant differences in obstetrical outcomes including GA at delivery, PPROM, PTB at <32 weeks, FLS-to-delivery duration or survival, including single/double fetal demise or single/double survival at birth, although the sample size appeared to be small (Table 3).

3.4 | Risk of bias assessment

The Newcastle-Ottawa Scale was used to assess risk of bias in included studies. All included studies had score of ≥7, except for one study which had score of 6 (total score in Table 1, details of scoring in Table S2).

3.5 | Sensitivity analysis and publication bias

No change of results were noted with leave-one-out analysis and no publication bias was noted by observing the funnel plots or using Begg's correlation test.

4 | DISCUSSION

This study provides an updated review of most up-to-date published case series and cohorts providing head-to-head comparison of TTTS pregnancies treated by FLS at <18 weeks vs ≥18 weeks and the subset of pregnancies treated at <16 weeks vs 16–18 weeks. This

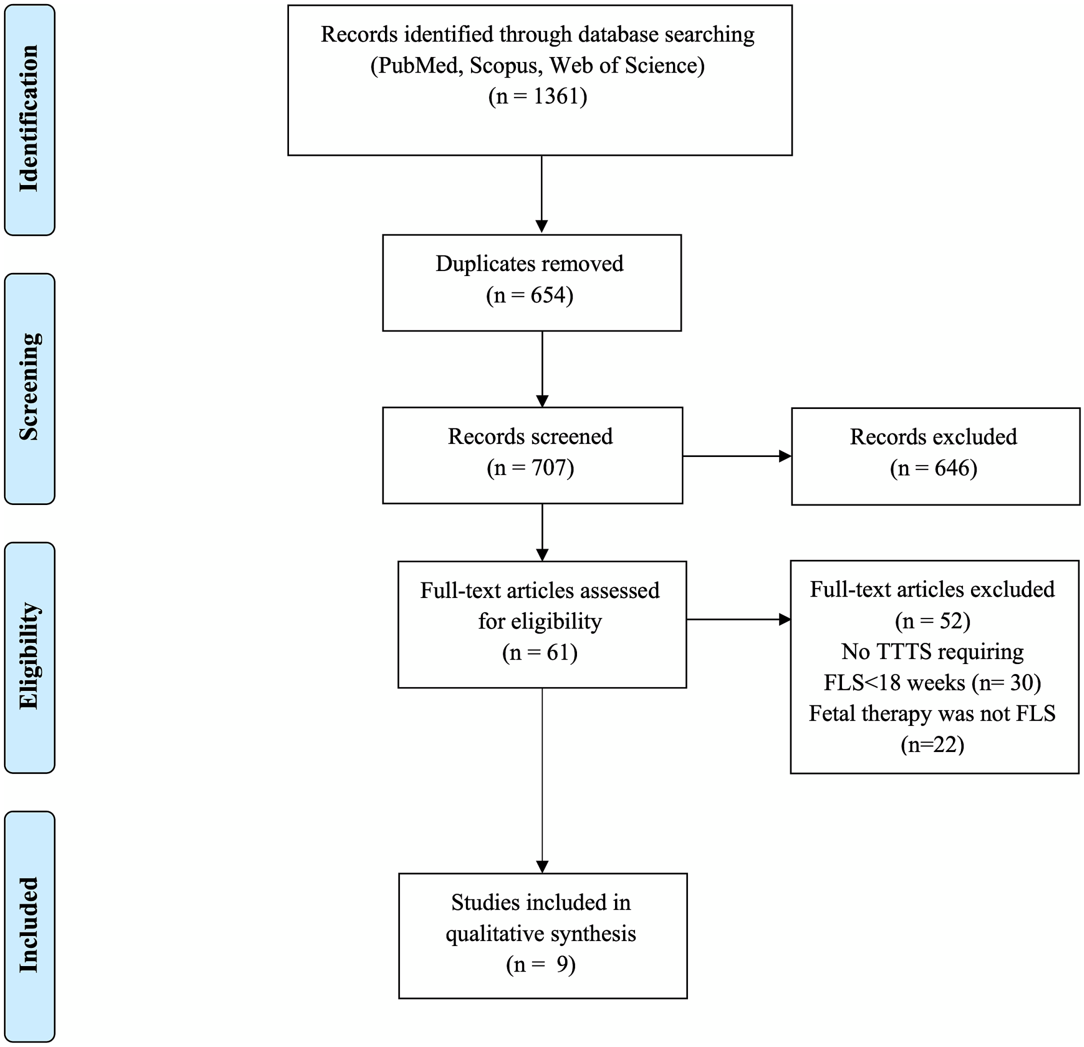

FIGURE 1 PRISMA flow chart of search and selection process.

study shows that TTTS stage III is more common in TTTS with FLS at <18 weeks and in the subset of TTTS at <16 weeks. GA at delivery was 3 weeks earlier in TTTS with FLS at <18 weeks than at ≥18 weeks. However, it was not significantly different in the subset of <16 weeks vs 16–18 weeks. There was no difference in outcomes including PPROM, PTB at <32 or <28 weeks, and in survival including fetal demise, live birth or neonatal survival, with similar findings in the subset that required laser surgery at <16 weeks.

Early development of TTTS comes with both diagnostic and therapeutic challenges. Most centers use GA-dependent cut-offs to define the deepest vertical pocket (DVP) of the recipient twin for the diagnosis of TTTS (>8 cm before and >10 cm after 20 weeks GA). Prior to 16 weeks of gestation, TTTS presentation might not be in accordance with Quintero staging and using this criterion causes underdiagnosing and underreporting of TTTS in early GA. By using the newly presented GA-specific reference range for measuring amniotic fluid in monochorionic/diamniotic twin pregnancies, a 6-cm DVP cut-off can be employed for diagnosing TTTS before 16 weeks of gestation.[34] Evaluation and monitoring of early TTTS at <16 weeks is also recommended to be done using maximal vertical pocket, Doppler parameters (UA A\REDF and DV A\R a-waves) and fetal echocardiography.[35]

The most discussed therapeutic challenge of early TTTS in the literature is the difficulty of performing FLS due to the lack of chorioamniotic fusion and the high risk of imposing PPROM and PTB in these fetuses.[14] PPROM is the most feared complication of FLS. Baud et al.[32] showed that the PPROM rate was inversely linked to the GA at FLS (<16 weeks 38%; 16–17 weeks 19%, and ≥17 weeks 6%), reflecting the degree of chorioamniotic fusion. Stirnemann et al.[14] also reported that pregnancies undergoing FLS at <17 weeks are at the highest risk of PPROM. Bearing the relatively small sample size of these studies in mind, larger studies are needed to help us understand whether the risk of PPROM is significantly higher in cases of early FLS. Potential strategies to reduce this rate of PPROM might be either the use of a smaller cannula (eg 10F) or delaying laser procedures until 17 weeks' gestation; the latter option must be weighed carefully against the potential adverse sequelae from progressive TTTS. However, studies did not show a significant difference in PTB or GA at delivery between different trocar sizes.[36,37]

TABLE 1 Characteristics of studies included in the systematic review.

Author	Study period	Country	Institution/Hospital	Study design	Study population (*n*)	Studied outcomes	No. total score
Bartin et al.[23]	2013–2020	France	Hôpital universitaire Necker-Enfants malades, Paris, France	Retrospective cohort	431	Cervical length, GA at delivery, PPROM, double and single fetal demise, double and single birth survival, double and single neonatal survival	9
Baud et al.[32]	1999–2012	Canada	Mount Sinai Hospital, Toronto, Ontario, Canada	Retrospective cohort	325	TTTS stages 1–4, anterior placenta, cervical length, procedure length, GA at intervention, PPROM, PPROM at <7 days after laser, PTB at <32 and 28 weeks' GA, delivery at <7 days after laser surgery, intervention-delivery days, GA at delivery, donor and recipient birthweight, donor and recipient fetal demise, double and single birth survival	8
Lecointre et al.[31]	2004–2012	France	Strasbourg University Hospitals, France	Prospective cohort	178	TTTS stages 1–4, GA at intervention, procedure length, anterior placenta, cervical length, GA at delivery, PPROM, PPROM at <7 days after laser surgery, PTB at <32 weeks GA, delivery at <7 days after laser surgery, intervention-delivery days, Donor and recipient birthweight, double and single fetal demise, donor and recipient fetal demise, double and single birth survival	7
Ortiz et al.[30]	2006–2011	Spain	Hospital Clínic, Barcelona, Spain	Retrospective cohort	270	Chorioamnion separation	8
Seaman et al.[21]	2012–2021	USA	Baylor University	Retrospective cohort	343	TTTS stages 1–4, anterior placenta, cervical length, chorioamnion separation, GA at delivery, pprom, intervention-delivery days, double and single birth survival, double and single neonatal survival	8
Sebire et al.[33]	1998–2005	UK	King's College Hospital, London, UK	Prospective cohort	83	GA at delivery, PTB at <32 and 28 weeks' GA, Delivery at <7 days after laser surgery, Intervention-delivery days, Double and single fetal demise, Donor and recipient fetal demise, Double and single birth survival	6
Sepulveda et al.[29]	2003–2006	Chile	Clinica Las Condes, Santiago, Chile	Prospective cohort	33	TTTS stage 3, GA at intervention, anterior placenta, GA at delivery, PTB at <32 and 28 weeks' GA, intervention-delivery days, double and single fetal demise, donor and recipient fetal demise, double and single birth survival, double and single neonatal survival	8
Tan et al.[20]	2019–2020	Malaysia	Hospital Raja Permaisuri Bainun, Ipoh, Perak, Malaysia	Retrospective cohort	17	TTTS stages 2–4, anterior placenta, procedure length, GA at delivery, PPROM, PPROM at <7 days after laser surgery, PTB at <32 and 28 weeks' GA, delivery at <7 days after laser, intervention-delivery days, double fetal demise, donor and recipient fetal demise, double and single birth survival, double and single neonatal survival	8
Willruth et al.[28]	2009	Germany	University of Bonn	Prospective case control	11	GA at delivery, PTB at <32 and 28 weeks' GA, intervention-delivery days, donor and recipient birthweight, single fetal demise, recipient fetal demise, double and single birth survival	8

Abbreviations: GA, gestational age; PPROM, preterm premature rupture of membranes; PTB, preterm birth; TTTS, twin-to-twin transfusion syndrome.

TABLE 2 Prenatal factors, obstetric outcomes and survival outcomes in pregnancies complicated with twin-to-twin transfusion syndrome that received fetoscopic laser surgery before 18 weeks compared with after 18 weeks.

Variable	Studies (*n*)	Laser for TTTS <18 weeks (*n/N*)	Laser for TTTS ≥18 weeks (*n/N*)	Overall OR (95% CI) or MD (95% CI)	I^2 (%)	*P* (*Z*)
Prenatal factors						
Maternal age	4[21,23,31,32]	213	1046	0.93 (−1.51 to 3.36)	48.5%	0.31
Nulliparity	3[23,31,32]	77/178	308/738	1 (0.47–2.12)	0.4%	1
TTTS stage I	3[21,31,32]	1/99	89/729	0.12 (0.02–1.01)	0.0%	0.05
TTTS stage II	4[20,21,31,32]	31/100	247/745	0.73 (0.23–2.26)	45.2%	0.44
TTTS stage III	5[20,21,29,31,32]	67/101	368/777	2.84 (1.24–6.54)	23.9%	**0.03**
TTTS stage IV	4[20,21,31,32]	2/100	61/745	0.57 (0.13–2.6)	0.0%	0.33
Anterior placenta	5[20,21,29,31,32]	40/101	343/777	0.84 (0.54–1.29)	0.0%	0.31
Cervical length (mm)	4[21,23,31,32]	213	1046	11.23 (−15.5 to 37.95)	35%	0.27
Cerclage	3[20,31,32]	1/65	28/437	0.67 (0.07–6.84)	0.0%	0.54
FLS duration (minutes)	3[20,31,32]	65	437	-5.27 (−9.19 to −1.34)	0.0%	**0.03**
Obstetric outcomes						
GA at delivery (weeks)	8[20,21,23,28,29,31–33]	220	1110	-3.12 (−6.11 to −0.13)	49.6%	**0.04**
PPROM	5[20,21,23,31,32]	79/202	344/1056	1.7 (0.77–3.75)	59.3%	0.14
PPROM <7 days after FLS	3[20,31,32]	6/65	37/437	2.2 (0.63–7.72)	0.0%	0.11
PTB <32 weeks' GA	6[20,28,29,31–33]	32/71	226/479	1.03 (0.59–1.79)	0.0%	0.89
PTB <28 weeks' GA	5[20,28,29,32,33]	10/31	91/341	1.39 (0.54–3.56)	0.0%	0.39
Delivery <7 days after FLS	4[20,31–33]	3/68	59/444	0.36 (0.07–1.9)	0.0%	0.15
FLS-to-Delivery (days)	7[20,21,28,29,31–33]	106	793	6.93 (−19.34 to 33.20)	41.9%	0.54
Survival outcomes						
Double fetal demise	6[20,23,29,31–33]	26/171	92/785	1.52 (0.96–2.39)	0.0%	0.06
Single fetal demise	6[23,28,29,31–33]	43/184	174/786	1.48 (0.46–4.73)	44.8%	0.43
Donor fetal demise	5[20,29,31–33]	23/69	157/476	1.37 (0.3–6.35)	32.9%	0.60
Recipient fetal demise	6[20,28,29,31–33]	20/71	114/485	1.26 (0.61–2.60)	0.0%	0.46
Double survival at birth	8[20,21,23,28,29,31–33]	138/220	715/1110	0.82 (0.40–1.68)	22.2%	0.53
Single survival at birth	8[20,21,23,28,29,31–33]	47/208	181/1104	2.1 (0.73–5.84)	57.0%	0.14
Double neonatal survival	4[20,21,23,29]	85/139	422/661	0.83 (0.59–1.17)	0.0%	0.19
Single neonatal survival	4[20,21,23,29]	37/139	160/661	1.17 (0.62–2.23)	0.0%	0.49

Abbreviations: CAS, chorioamnion separation; FLS, fetoscopic laser surgery; GA, gestational age; MD, mean difference; PPROM, preterm premature rupture of membranes; PTB, preterm birth; TTTS, twin-to-twin transfusion syndrome.
Bold values indicate statistical significance.

The results of our meta-analysis showed no significant difference in the rate of PPROM among early TTTS cases undergoing FLS at <16 and 16–18 weeks' GA. As the major challenge in TTTS, PTB is the most important risk factor for neonatal mortality and morbidity, particularly neurodevelopmental disabilities.[38] A recent study by Bartin et al.[23] showed that PTB at <28 weeks is significantly related to the GA at FLS and impacts neonatal morbidity among survivors.[23] In this study the rate of PTB at <28 weeks did not differ among cases of TTTS that underwent FLS at <18 or ≥18 weeks of GA (OR 1.39, 95% CI 0.54–3.56).

Experts consider FLS the best management approach for stage II–IV TTTS at <26 weeks' GA, but there are controversies regarding its feasibility at <16 weeks.[39] For cases of early TTTS at <16 weeks, a recently published Delphi study suggests expectant management for TTTS stage ≤2 when maternal symptoms such as shortness of breath, contractions and cervical length <20 mm are absent – and FLS for stage ≥3 when the procedure is technically possible.[35] In the subgroup analysis of TTTS cases who had undergone FLS at <16 weeks compared with those who had FLS between 16 and 18 weeks, perinatal mortality rates did not differ (Table 3). A recent study on perinatal outcomes following FLS at <16 weeks of pregnancy showed an association between early FLS and significantly higher rates of chorioamniotic separation, PPROM and chorioamnionitis, but no negative impact on survival.[21]

The strengths of this review are the thorough search and assessment of three large databases. We acknowledge the limitations of our study. The small number of cases in some of the included studies, their retrospective non-randomized design, heterogeneity in prenatal management and different follow-up periods represent this systematic review's major

TABLE 3 Prenatal factors, obstetric outcomes and survival outcomes in pregnancies complicated with twin-to-twin transfusion syndrome that received fetoscopic laser surgery before 16 weeks compared with 16–18 weeks.

Variable	Studies (*n*)	Laser for TTTS <16 weeks (*n*/*N*)	Laser for TTTS 16–18 weeks (*n*/*N*)	Overall OR (95% CI) or MD (95% CI)	I^2 (%)	*P* (*Z*)
Prenatal factors						
TTTS stage II	2[31,32]	5/19	22/45	0.38 (0.09–)	0.0%	0.07
TTTS stage III	2[31,32]	14/19	22/45	2.95 (1.62–5.35)	0.0%	**0.03**
Anterior placenta	2[31,32]	8/19	15/45	1.45 (0.02–119.21)	0.0%	0.48
Obstetrical outcomes						
GA at delivery (weeks)	3[31–33]	20	47	−0.84 (−5.59 to 3.91)	0.0%	0.53
PPROM	2[31,32]	4/19	17/45	0.31 (0.04–2.56)	0.0%	0.09
PTB <32 weeks GA	3[31–33]	10/20	20/47	1.25 (0.21–7.46)	0.0%	0.64
FLS-to-Delivery (days)	3[31–33]	20	47	12.88 (−60.18 to 85.93)	40.8%	0.53
Survival outcomes						
Double fetal demise	3[31–33]	5/20	6/47	1.76 (0.03–117.63)	44.7%	0.62
Single fetal demise	3[31–33]	5/20	12/47	0.91 (0.27–3.1)	0.0%	0.77
Donor fetal demise	2[31,32]	7/19	12/45	1.56 (0.01–216.88)	0.0%	0.46
Recipient fetal demise	3[31–33]	7/20	11/47	1.43 (0.03–59.94)	44.6%	0.72
Double survival at birth	2[31,32]	9/19	29/45	0.51 (0.01–48.5)	0.0%	0.31
Single survival at birth	3[31–33]	5/20	12/47	0.91 (0.27–3.1)	47.0%	0.14

Abbreviations: FLS, fetoscopic laser surgery; GA, gestational age; MD, mean difference; PPROM, preterm premature rupture of membranes; PTB, preterm birth; TTTS, twin-to-twin transfusion syndrome.
Bold values indicate statistical significance.

limitations. Some of the variables that we intended to collect and stratify were only reported by limited studies, limiting our ability to include them in the analysis. Successful fetoscopic laser surgery relies on understanding and executing the various technical aspects. This is particularly true for laser surgery for early TTTS, which is generally regarded as technically challenging. The findings are also subject to potential publication bias because the nature of some outcomes and the small number of studies limits the reliability of formal tests. As international guidelines suggest performing biweekly sonographic screening for TTTS from 16 weeks onwards,[8] early TTTS at <16 weeks might be underreported in the available literature. The potential of selection bias also exists favoring FLS rather than expectant management, amnioreduction or selective reduction for patients with technically feasible surgeries.

5 | CONCLUSION

Our results indicate that despite the excess of more severe TTTS cases, laser surgery at 16–18 weeks of gestation for the management of TTTS does not result in excessive preterm deliveries, PPROM or reduced neonatal survival when compared with laser surgery at or after 18 weeks. These observations could be useful in determining when to perform laser photocoagulation on the placental anastomoses in cases of advanced early TTTS diagnosed before 18 weeks of gestation. It appears that fetoscopic laser surgery is feasible and is not associated with an increased risk of perinatal death in the subset of TTTS pregnancies that are >16 weeks' gestation. Nonetheless, it is important to interpret the available data with caution, since they are based on small studies. Future studies should use standardized definitions and objective protocols for prenatal diagnosis and treatment to estimate clinically relevant perinatal outcomes more accurately.

CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Mustafa HJ, Aghajani F, Patrick E, Baerz MM, Arias-Sánchez P, Khalil A. Perinatal outcomes following fetoscopic laser surgery for early twin-to-twin transfusion syndrome: Systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2024;00:1-8. doi:10.1111/aogs.14806