Timing of intra-fetal laser therapy for twin reversed arterial perfusion (TRAP) sequence: Retrospective series and systematic review and meta-analysis

Annachiara Vitucci | Nicola Fratelli | Anna Fichera | Enrico Sartori | Federico Prefumo

Division of Obstetrics and Gynecology, ASST Spedali Civili and Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

Correspondence
Federico Prefumo, Division of Obstetrics and Gynecology, ASST Spedali Civili, Piazzale Spedali Civili 1, 25123 Brescia, Italy. Email: federico.prefumo@unibs.it

Abstract
Objective: To estimate the neonatal survival rate after intra-fetal laser (IFL) treatment for twin reversed arterial perfusion (TRAP) sequence, and to investigate the effect of gestational age at the time of procedure.

Methods: Retrospective cohort study of TRAP sequences followed at our institution from 2013–2020. Systematic review and meta-analysis of the neonatal survival rate after IFL was conducted. Both diamniotic and monoamniotic monochorionic pregnancies were included. A subgroup analysis to compare outcomes according to gestational age at procedure (<16^{+}0 weeks or ≥16^{+}0 weeks) was planned.

Results: Thirteen pregnancies were followed at our center and seven were treated with IFL: the survival rate was 57%. Ten studies published between 2008 and 2020 for a total of 156 cases were included in the meta-analysis. The overall neonatal survival after IFL was 79% (95% CI 0.72–0.86, I^2 22%). A random-effects model comparing neonatal survival for IFL performed <16^{+}0 weeks versus ≥16^{+}0 weeks showed no significant difference between the two groups (OR = 0.93; 95% CI 0.37–2.33).

Conclusion: IFL is a safe and minimally invasive technique for the treatment of TRAP sequence, with a survival rate of 79%. Gestational age at treatment (before or after 16 weeks) does not seem to affect neonatal survival rate.

KEYWORDS
fetal therapy, interstitial laser, meta-analysis, monochorionic twins, systematic review, TRAP sequence

1 INTRODUCTION

Twin reversed arterial perfusion (TRAP) sequence is a unique complication of monochorionic multiple pregnancy in which an acardiac twin with multiple morphological anomalies and without a complete cardiovascular system is perfused by a structurally normal co-twin (the pump twin).^ The acardiac twin is not viable, but it endangers the pump twin, causing an increased risk of congestive heart failure, intrauterine growth restriction (IUGR), preterm premature rupture of membranes (pPROM) and preterm delivery. The main goals in TRAP sequence management are preserving the survival of the pump twin and approaching a term delivery. If a conservative management is
not advisable, the treatment consists of stopping blood supply to the acardiac twin. Among such devascularization techniques, intra-fetal laser (IFL) treatment has gained momentum in recent years, due to its minimal invasiveness and the possibility to perform it as early as the first trimester of pregnancy. However, there is ongoing debate regarding the best timing of the procedure, and its relative safety at early gestational ages.

The first aim of this study was to review our center’s experience in the management and treatment with IFL of monochorionic twin pregnancies complicated by TRAP sequence. The second aim was to perform a systematic review of the literature on pump twin neonatal survival after IFL treatment, with a planned subgroup analysis according to the timing of intervention (before 16\textsuperscript{th} weeks versus at or more than 16\textsuperscript{th} weeks).

2 | MATERIALS AND METHODS

2.1 | Cohort study

This retrospective study reviewed all consecutive cases of monochorionic twin pregnancies referred to ASST Spedali Civili of Brescia between January 2013 (when we switched from radiofrequency ablation to IFL) and December 2020 because of a suspicion or a diagnosis of TRAP sequence. Data were retrieved by searching the computerized ultrasound database. In case of missing data about pregnancy outcomes, the woman or referring physician were contacted. As this was a retrospective audit of anonymized data, no ethics committee approval was necessary according to national regulations; all women gave their written consent to use their routinely collected hospital data for retrospective studies without patient identifiers. Gestational age was confirmed in all cases by a first trimester ultrasound scan measuring the crown to rump length (CRL) of the pump twin. Chorionicity and amnionicity were assessed in the first trimester. At the first evaluation in our center, the diagnosis of TRAP sequence was confirmed by an ultrasound scan using color Doppler in the presence of an acardiac twin receiving a retrograde blood flow from the pump twin. All patients were counselled about the clinical significance of TRAP sequence, the natural history of this condition and the possibility of termination of pregnancy. We offered fetal therapy in cases in which a significant risk of death for the pump twin was assessed: persistent blood flow to the acardiac twin and an acardiac estimated fetal weight larger than 50% of the pump twin or an initial overload of pump twin indicated by mild polyhydramnios or ductus venous pulsatility index for veins (DV-PIV) >95th centile. The main techniques used were fetoscopic cord coagulation and transection of the acardiac umbilical cord (COT) and interstitial IFL. Interventional procedures were performed only by two different operators with more than 10 years’ experience. Patients were admitted to the hospital the day before or the same day of the treatment in the early morning. They had been fasting for 6 h prior to the procedure. Before starting intervention, they received prophylactic antibiotics with i.v. cephalosporins; conscious sedation with midazolam i.v. and local anesthesia with mepivacaine were also performed.

COT was adopted in monochorionic monoamniotic (MCMA) pregnancies at risk of cord entanglement. In all remaining cases in which fetal therapy was indicated, IFL was performed. Under ultrasound guidance, an 18-gauge needle was inserted with a free-hand technique in the pelvis of the acardiac twin, very close to the intra-abdominal portion of the feeding vessels (umbilical artery and vein in proximity of the hilum); then, a 600-μm laser fiber was inserted into the needle and advanced a few millimeters in front of the needle tip. Laser coagulation was obtained with a diode laser generator. The initial power was set at 10 W to avoid thermal injury to the surrounding tissues. Multiple impulses of a few seconds were repeated until the tissue near the laser fiber became hyperechoic; when the cessation of reverse perfusion in the acardius was detected by color Doppler, the procedure was considered complete.

The day after the procedure, an ultrasound examination was performed to check the heart activity in the pump twin and to confirm the absence of reverse flow through the acardiac twin. Women were discharged in the absence of vaginal bleeding, amniotic fluid losses or uterine contractions. Ultrasound follow-up was planned after 1 week at our center, and in the referring hospital thereafter.

2.2 | Systematic review

The review was performed following an a-priori protocol (https://www.crd.york.ac.uk/prospero/display_record.php?RecID=211452) and is reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement and checklist. The study was registered with the PROSPERO database (registration number: CRD42020211452). The quality of the articles included in the review was assessed using the Newcastle-Ottawa Scale. Medline, EMBASE and clinicaltrials.gov were searched on the 1 December 2020 using the following keywords: ‘TRAP sequence’, ‘laser’, ‘interstitial’, ‘intrafetal’. Reference lists of relevant articles and reviews were manually searched. Two trained reviewers (A.V. and F.P.) independently screened titles and abstracts for relevance. The full text of relevant articles was evaluated independently and agreement about potential eligibility was reached by consensus. We included reports in English language about treatment of TRAP sequence by IFL that provided data on survival of the pump twin. Prospective and retrospective cohort studies, case-control studies and case series were included; editorialials, case reports and personal communication were excluded. Only series with five or more cases were taken into account; we did not include smaller series in order to minimize selection bias. In case of data duplication, only the most recent and complete work was included. Discordance was resolved with consensus. An effort was made to obtain missing data by contacting the corresponding author of the publications; we subsequently excluded studies with incomplete outcomes of the cases. For each study we collected data on gestational age at IFL, pPROM, intrauterine fetal demise, gestational age at delivery, and neonatal survival.
A random-effects model was used to estimate weighted neonatal survival rates with 95% confidence intervals due to the heterogeneity between studies. We did not formally test for publication bias, given the low power of testing with the small number of studies included. All analyses were performed with the statistical software OpenMetaAnalyst.  

3 | RESULTs  

3.1 | Cohort study  

In the study period, 15 women were referred to our center with a suspicion of TRAP sequence. Six pregnancies were MCMA and nine pregnancies were monochorionic diamniotic (MCDA). We confirmed the diagnosis of TRAP sequence in all cases. Details about the cohort are available in Table S1. The patient flow-chart is reported in Figure S1.  

Eleven cases were considered eligible for treatment. In two cases of MCMA pregnancies, because of a long cord of the parasitic twin and the subsequent presence of cord entanglement, the treatment chosen was COT. The pregnancies delivered at 30±5 and 33±1 weeks, and both babies survived.  

Nine patients were eligible for IFL treatment. On the day scheduled for the procedure, unfortunately two pump fetuses were found without cardiac activity (at 15±1 and 18±3 weeks, respectively); these fetuses had shown a reversed ductus venous A wave in the ultrasound examination preceding surgery. Seven pregnancies were treated with IFL at a mean gestational age of 15±5 weeks (range 12±3–19±5 weeks). Four pregnancies were MCDA and three MCMA without evidence of cord entanglement. In two cases, both MCMA, fetal demise was diagnosed at follow-up (1 and 54 days after the procedure). In three MCDA cases the pregnancy was uneventful, laser treatment was performed, and three healthy babies were delivered at term. In another MCDA pregnancy, IFL treatment was performed at 20±2 weeks. The day after the procedure, the pump twin presented a DV-PIV >95th centile, that was not detected at the following examinations. At 26±1 weeks, the woman was admitted because of reduction of fetal movements. An emergency cesarean section for abnormal cardiotocography was performed at 26±2 weeks. A baby girl of 684 g was born; she was discharged from the neonatal intensive care unit without major morbidities, and is presently in good health.  

In another MCMA pregnancy, the gestational age at procedure was 13±5 weeks. Cord coagulation and transection was excluded because of a body stalk anomaly of the acardius. During ultrasound follow-up in the referring hospital, a retrochorionic hematoma was detected; because of heavy vaginal bleeding an emergency cesarean section was performed at 24±5 weeks; the baby died on the following day.  

Overall, we observed a 57% rate of neonatal survival rate (4/7) in the IFL treatment group. Details of the cases are shown in Table S2.  

3.2 | Systematic review  

We included in our systematic review a total of nine studies which met the selection criteria (Figure 1), plus our current series. Newcastle-Ottawa Scale quality assessment is shown in Table 1: a maximum score of 9 can be assigned, based on selection (maximum 4), comparability (maximum 2) and outcome (maximum 3) items. In order to limit confounding bias, data about triplets were excluded from the meta-analysis. Outcomes of the 11 triplet pregnancies treated with IFL are separately reported in Table S3. The meta-analysis population included 156 monochorionic twin pregnancies complicated by TRAP sequence undergoing IFL. Data on pregnancy outcomes (survival or intrauterine demise of the pump twin) and gestational age at treatment are reported in Table S4. The overall neonatal survival rate of the pump twin estimated from meta-analysis was 79% (95% CI 0.72–0.86, I² 22%). The Forest plot is reported in Figure 2a.  

We further divided the IFL therapy cohort into two groups, according to the gestational age at treatment: at less than 16.5 weeks (early treatment group), and at 16 or more weeks of gestational age (late treatment group). Data about gestational age at delivery, pPROM and days between procedure and intrauterine demise of pump twin were incomplete; we report the available ones in Tables 2 and 3. The early treatment group included 60 pregnancies treated at a weighted mean gestational age of 13±5 weeks. In the late treatment group, 96 pregnancies were treated at a weighted mean gestational age of 19±6 weeks. The overall survival for each group was calculated trough a pooled proportion random-effects model, as shown in Figure 2b,c.  

A meta-analysis (through a random-effects model) comparing the neonatal survival OR in each study showed no statistically significant difference between the two groups (OR = 0.927; 95% IC 0.37–2.33). Results are shown in Figure 3.  

4 | DISCUSSION  

We found that the neonatal survival rate of the pump twin after IFL for TRAP is approximately 80%. Timing of IFL (before or after 16 weeks of gestation) is not associated with differences in neonatal survival rate.  

The major limitations of our systematic review are the small number of studies included and their retrospective non-randomized design. Indications for IFL treatment were not homogeneously reported in all studies and may have differed between studies and in the same study over time. One single study contributed almost one third of the total cases, and 45% of those treated at or more than 16 weeks.  

Several studies and reviews of literature tried to identify the technique of choice in TRAP treatment. Radiofrequency ablation (RFA) and IFL are currently the most commonly used techniques due to their reliability and safety. The previously published experience in TRAP sequence treatment at our center reported the use...
of RFA and reviewed the existing literature: six studies were included for a total of 78 pregnancies (monochorionic twins or triplets with a monochorionic component). The overall neonatal survival in TRAP sequence treated by RFA was 85%. A rough pPROM rate was estimated at 22% (19/85), since not all studies reported specific details. Other large cohorts reported pump twin survival rates of 70%–80%.

The other technique that appeared feasible since its first description by Jolly et al. is IFL. Several publications have investigated its rate of success and the related outcomes of pregnancy. Overall neonatal survival rate was 80% in the systematic review by Pagani et al. based on 51 cases, and 76% in the one by Chaveeva et al. based on 104 pregnancies. Regarding the comparison between RFA and IFL, Pagani et al. noted that, even though neonatal survival rate was similar, pPROM before 32 weeks’ gestation was more common with RFA. Chaveeva suggested that the risk of death for the pump twin using IFL is lower if treatment is undertaken at 12–14 weeks than at later gestational ages. A real comparison between RFA and IFL is not possible at such early gestational ages, since RFA is rarely performed before 15 weeks.
At our center, in the last 6 years the technique of choice has been IFL, because of the possibly lower rate of complications and easier availability of the laser generator. In our series, we had a 57% neonatal survival rate, 29% of late post-procedure fetal demise and 14% perinatal death rate. As opposed to RFA, we did not observe pPROMs after IFL, which is in keeping with the findings of Pagani et al. The overall neonatal survival rate in our series was lower than other previously published studies. Possible reasons of this difference can be the small sample size and the presence in the treatment group of three MCMA pregnancies in which we observed the
| Study                          | N. cases treated <16\(^{+0}\) | Mean GA at treatment (range) | N. pump alive (%) | Mean GA at delivery (range) | N. pPROM (%) | N. pump IUFD (%) | N. pump neonatal death |
|-------------------------------|--------------------------------|-------------------------------|------------------|-----------------------------|-------------|-----------------|----------------------|
| O'Donoghue et al. 2008        | 5                              | 14\(^{+2}–\)15\(^{+5}\)       | 4 (80%)          | 38\(^{+2}–\)39\(^{+3}\)   | 1 (20)      | 1 (20)          | 0                    |
| Scheier and Molina 2012       | 2                              | 13\(^{+1}–\)13\(^{+9}\)       | 2 (100%)         | 39\(^{+4}–\)40\(^{+4}\)   | 0           | 0               | 0                    |
| Pagani et al. 2013            | 6                              | 14\(^{+2}–\)15\(^{+5}\)       | 5 (83%)          | 38\(^{+1}–\)40\(^{+5}\)   | 0           | 1 (17)          | 0                    |
| Berg et al. 2014              | 8                              | 14\(^{+3}–\)15\(^{+6}\)       | 6 (75%)          | 38\(^{+3}–\)40\(^{+6}\)   | 0           | 2 (25)          | 0                    |
| Chaveeva et al. 2014          | 9                              | 13\(^{+0}–\)14\(^{+4}\)       | 6 (66.6%)        | 39\(^{+0}–\)40\(^{+6}\)   | NR          | 3 (33.4)        | 0                    |
| Roethlisberger et al. 2017    | 12                             | 12\(^{+2}–\)13\(^{+5}\)       | 7 (58.3%)        | 40\(^{+5}–\)40\(^{+6}\)   | 0           | 5 (41.7)        | 0                    |
| Tavares de Sousa et al. 2020  | 12                             | 12\(^{+2}–\)13\(^{+5}\)       | 11 (91.7%)       | 39\(^{+2}–\)42\(^{+1}\)   | 0           | 1 (8.3)         | 0                    |
| Shettikeri et al. 2020        | 1                              | 15\(^{+0}\)                   | 1 (100%)         | NR                          | 0           | 0               | 0                    |
| Seshadri et al. 2020          | -                              | -                             | -                | -                          | -           | -               | -                    |
| Present study                 | 5                              | 13\(^{+5}–\)14\(^{+1}\)       | 2 (40%)          | 33\(^{+6}–\)39\(^{+5}\)   | 0           | 2 (40)          | 1                    |
| Total                         | 60                             | 13\(^{+5}\)                   | 44               |                            |             |                 | 16                   |

Abbreviations: GA, gestational age; pPROM, preterm premature rupture of membranes; IUFD, intrauterine fetal death; NR, not reported.
of pregnancy complications was not possible. Consequently, given the risk of spontaneous pump twin loss with delayed procedures, our data may suggest an advantage for early treatment of TRAP sequence. However, this finding must be interpreted with caution, since timing of the procedures in non-randomized studies is influenced by several unmeasured confounders related to operator’s experience and judgment, patient’s preference, and of course gestational age at referral.

In conclusion, IFL is a safe and minimally invasive technique that allows a satisfactory treatment of TRAP sequence. Gestational age at treatment (before or after 16 weeks) does not seem to affect neonatal survival rate. This would favor early treatment but needs to be confirmed by ongoing randomized controlled studies.

ACKNOWLEDGMENTS
Open Access Funding provided by Universita degli Studi di Brescia within the CRUI-CARE Agreement.
[Correction added on 08-May-2022, after first online publication: CRUI-CARE funding statement has been added.]

CONFLICT OF INTEREST
The authors have no conflict of interest to declare.

AUTHOR CONTRIBUTIONS
AV, AF and FP conceived and designed this study. AV, NF, AF and FP contributed substantially to the acquisition of the data. AV and FP performed statistical analyses. AV, NF, AF, ES and FP contributed to the interpretation of the results. AV and FP drafted the paper. AV, NF, AF, ES and FP revised and approved the final version of the manuscript.

TABLE 3  Outcomes with IFL treatment at ≥16^{+0} weeks of gestation

| Study                     | N. cases treated ≥16^{+0} | Mean GA at treatment (range) | N. pump alive (%) | Mean GA at delivery (range) | N. pPROM (%) | N. pump IUFD (%) | N. pump neonatal death |
|---------------------------|---------------------------|-------------------------------|-------------------|-----------------------------|--------------|-----------------|------------------------|
| O’Donoghue et al. 2008    | 5                         | 18^{+6} (16^{+6}-20^{+5})    | 2 (40)            | 34^{+1} (30^{+2}-38^{+6})  | 0            | 3 (60)          | 0                      |
| Scheier and Molina 2012   | 5                         | 17^{+5} (16^{+2}-20^{+3})    | 4 (80)            | 36^{+0} (29^{+2}-39^{+3})  | 1 (20%)      | 1 (20)          | 0                      |
| Paganì et al. 2013        | 10                        | 21^{+6} (17^{+4}-25^{+6})    | 8 (80)            | 34^{+6} (27^{+5}-38^{+0})  | 0            | 2 (20)          | 0                      |
| Berg et al. 2014          | 3                         | 17^{+3} (16^{+0}-20^{+6})    | 2 (66.6)          | 38^{+5} (36^{+3}-40^{+6})  | 0            | 1 (33.4)        | 0                      |
| Chaveeva et al. 2014      | 43                        | 19^{+0} (16^{+0}-24^{+0})    | 34 (79.1)         | 36^{+0} (26^{+0}-42^{+3})  | NR           | 9 (20.9)        | 0                      |
| Roethlisberger et al. 2017| –                         | –                             | –                  | –                           | –            | –               | –                      |
| Tavares de Sousa et al. 2020| –                        | –                             | –                  | –                           | –            | –               | –                      |
| Shettikeri et al. 2020    | 6                         | 19^{+6} (16^{+6}-30^{+6})    | 6 (100)           | NR                          | 0            | 0               | 0                      |
| Seshadri et al. 2020      | 22                        | 22 (16^{+0}-26^{+3})         | 16 (73)           | 37^{+0} (36^{+1}-38^{+0})  | 2 (9%)       | 5 (22)          | 1                      |
| Present study             | 2                         | 18^{+6} (17^{+1}-20^{+2})    | 2 (100)           | NR                          | 0            | 0               | 0                      |
| Total                     | 96                        | 19^{+6}                       | 74                | 3                           | 21           | 1               |                        |

Abbreviations: GA: gestational age; pPROM: preterm premature rupture of membranes; IUFD: intrauterine fetal death; NR: not reported.

FIGURE 3  Forest plot for subgroup analysis (early treatment at <16^{+0} weeks of gestation versus late treatment at ≥16^{+0} weeks of gestation) of overall intrafetal laser treatment neonatal survival

INFORMED CONSENT
Written consent was obtained from all women.
DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

ORCID

Anna Fichera http://orcid.org/0000-0002-7368-0823
Federico Prefumo https://orcid.org/0000-0001-7793-714X

REFERENCES

1. Vitucci A, Fichera A, Fratelli N, Sartori E, Prefumo F. Twin reversed arterial perfusion sequence: current treatment options. Int J Womens Health. 2020;12:435-443.
2. Jolly M, Taylor M, Rose G, Govender L, Fisk NM. Intestinal laser: a new surgical technique for twin reversed arterial perfusion sequence in early pregnancy. BJOG. 2001;108:1098-1102.
3. Roethlisberger M, Striezek B, Gottschalk I, et al. First-trimester intervention in twin reversed arterial perfusion sequence: does size matter? Ultrasound Obstet Gynecol. 2017;50:40-44.
4. Tavares de Sousa M, Glosemeyer P, Diemert A, Bamberg C, Hecher K. First-trimester intervention in twin reversed arterial perfusion sequence. Ultrasound Obstet Gynecol. 2020;55:47-49.
5. Prefumo F, Fichera A, Zanardini C, Frusca T. Fetoscopic cord transaction for treatment of monoamniotic twin reversed arterial perfusion sequence. Ultrasound Obstet Gynecol. 2014;43:234-235.
6. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
7. Wells G, Shea B, O’Connell D, Peterson J, Welch V, Losos M, et al. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
8. Centre for Reviews and Dissemination. Systematic Reviews: CRD’s Guidance for Undertaking Reviews in Health Care. University of York; 2009.
9. Wallace BC, Dahabreh IJ, Trikalinos TA, Lau J, Trow P, Schmid CH; 2012-2012:49; 15, Closing the gap between methodologists and end-users: Ras a computational Back-end.
10. O’Donoghue K, Barigye O, Pasquini L, Wimalasundera RC, Fisk NM. Intestinal laser therapy for fetal reduction in monochorionic multiple pregnancy: loss rate and association with aplasia cutis congenita. Prenat Diagn. 2008;28:535-543.
11. Scheier M, Molina FS. Outcome of twin reversed arterial perfusion sequence following treatment with intestinal laser: a retrospective study. Fetal Diagn Ther. 2012;31:35-41.
12. Berg C, Holst D, Mallmann MR, Gottschalk I, Geipel A. Early vs late intervention in twin reversed arterial perfusion sequence. Ultrasound Obstet Gynecol. 2014;43:60-64.
13. Pagani G, D’Antonio F, Khalil A, Papageorgiou A, Bhide A, Thilaganathan B. Intrafetal laser treatment for twin reversed arterial perfusion sequence: cohort study and meta-analysis. Ultrasound Obstet Gynecol. 2013;42:6-14.
14. Chaveeva P, Poon LC, Sotiriadis A, Kosinski P, Nicolaides KH. Optimal method and timing of intrauterine intervention in twin reversed arterial perfusion sequence: case study and meta-analysis. Fetal Diagn Ther. 2014;35:267-279.
15. Shettiker A, Acharya V, V S, Sahana R, Radhakrishnan P. Outcome of pregnancies diagnosed with TRAP sequence prenatally: a single-Centre experience. Fetal Diagn Ther. 2020;47:301-306.
16. Seshadri S, Shinde RR, Ram U. Intrafetal laser for midtrimester TRAP sequence-experience from a single center. Prenat Diagn. 2020;40:885-891.
17. Cabassa P, Fichera A, Prefumo F, et al. The use of radiofrequency in the treatment of twin reversed arterial perfusion sequence: a case series and review of the literature. Eur J Obstet Gynecol Reprod Biol. 2013;166:127-132.
18. Zhang ZT, Yang T, Liu CX, Li N. Treatment of twin reversed arterial perfusion sequence with radiofrequency ablation and expectant management: a single center study in China. Eur J Obstet Gynecol Reprod Biol. 2018;225:9-12.
19. Lee H, Bebbington M, Crombleholme TM. The north American fetal therapy network registry data on outcomes of radiofrequency ablation for twin-reversed arterial perfusion sequence. Fetal Diagn Ther. 2013;33:224-229.
20. Valsky DV, Martinez-Serrano MJ, Sanz M, et al. Cord occlusion followed by laser cord transection in monochorionic monoamniotic discordant twins. Ultrasound Obstet Gynecol. 2011;37:684-688.
21. Lee H, Wagner AJ, Sy E, et al. Efficacy of radiofrequency ablation for twin-reversed arterial perfusion sequence. Am J Obstet Gynecol. 2007;196(459):e451-e454.
22. Peeters SH, Devlieger R, Middeldorp JM, et al. Fetal surgery in complicated monoamniotic pregnancies: case series and systematic review of the literature. Prenat Diagn. 2014;34:586-591.
23. Lewi L, Valencia C, Gonzalez E, Deprest J, Nicolaides KH. The outcome of twin reversed arterial perfusion sequence diagnosed in the first trimester. Am J Obstet Gynecol. 2010;203(213):e211-e214.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.

How to cite this article: Vitucci A, Fratelli N, Fichera A, Sartori E, Prefumo F. Timing of intra-fetal laser therapy for twin reversed arterial perfusion (TRAP) sequence: Retrospective series and systematic review and meta-analysis. Int J Gynecol Obstet. 2022;159:833-840. doi: 10.1002/ijgo.14221