First-trimester intervention in twin reversed arterial perfusion sequence

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CONTRIBUTION
What are the novel findings of this work?
Early intrafetal laser therapy in pregnancy with twin reversed arterial perfusion (TRAP) sequence does not increase fetal-loss rate, resulting in 92% live births, and it may be advantageous in comparison to waiting until a more advanced gestational age. Our findings are in partial contrast to those of a previously published study, in which fetal-loss rate was comparatively high at 42%.

What are the clinical implications of this work?
Our findings support first-trimester interstitial laser therapy in pregnancy complicated by TRAP sequence, being associated with a live-birth rate of 92%.

ABSTRACT
Objective To report the outcome of monochorionic twins with twin reversed arterial perfusion (TRAP) sequence following interstitial laser therapy in the first trimester.

Methods This was a retrospective cohort study of all consecutive cases of TRAP that underwent interstitial laser therapy at ≤14+3 weeks’ gestation between January 2014 and April 2016. Interstitial laser treatment was performed under ultrasound guidance using a 400-nm Nd:YAG laser fiber. Hospital records were reviewed to ascertain perinatal survival and morbidity.

Results Twelve monochorionic twin pregnancies underwent interstitial laser treatment of the umbilical artery of the acardiac fetus, at a median gestational age of 13 + 5 (interquartile range (IQR), 13 + 4 to 14 + 0) weeks. In all cases, one treatment was sufficient to achieve complete interruption of the perfusion of the acardiac twin. There were no procedure-related complications during or within 48 h after the procedure. In one (8.3%) case, intrauterine death of the pump twin occurred 2 weeks after the intervention. All other cases (91.7%) resulted in a live birth at a median gestational age of 39 + 6 (IQR, 37 + 1 to 41 + 2) weeks and with a median birth weight of 3370 (IQR, 2980–3480) g. No neonatal mortality or serious morbidity occurred.

Conclusions Our results support the use of interstitial laser therapy in the first trimester of pregnancy complicated by TRAP sequence, showing a live birth rate of 92%. The results of a randomized controlled trial, evaluating early vs late intervention in pregnancy with TRAP sequence, are awaited. © 2019 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of the International Society of Ultrasound in Obstetrics and Gynecology.

INTRODUCTION
Twin reversed arterial perfusion (TRAP) occurs in up to 2.6% of monochorionic twin pregnancies. In 1900, Schatz described a reversed circulation in the acardiac twin associated with a large artery-to-artery and vein-to-vein anastomosis between the pump twin and the acardius. Accordingly, the pump twin carries the burden of perfusing the acardiac twin, which results in a mortality rate of up to 55% due to cardiac failure or preterm delivery caused by polyhydramnios. The only causal treatment of TRAP sequence is interruption of the blood flow to the acardiac twin. Several fetoscopic techniques have been described, including cord coagulation, cord ligation and photocoagulation of the anastomoses, as well as intrafetal methods such as radiofrequency ablation and intrafetal laser therapy. The only causal treatment of TRAP sequence is interruption of the blood flow to the acardiac twin. Several fetoscopic techniques have been described, including cord coagulation, cord ligation and photocoagulation of the anastomoses, as well as intrafetal methods such as radiofrequency ablation and intrafetal laser therapy.

Optimal timing of therapy has yet to be established. Lewi et al. demonstrated a loss rate of 8/24 (33%) between...
diagnosis of TRAP in the first trimester and planned intervention at 16–18 weeks' gestation and Pagani et al. reported an unexpectedly high (5/6) spontaneous loss rate at a median gestational age of 14 + 4 weeks in a conservatively managed group. Early intervention in pregnancies with TRAP sequence became possible with the introduction of ultrasound-guided intrafetal laser ablation (IFL) of the perfusion to the acardiac twin. Roethlisberger et al. evaluated the outcome after first-trimester intervention by IFL of 12 cases complicated by TRAP, and showed that ablation of the feeding vessels before 14 + 0 weeks' gestation resulted in intrauterine death of 5/12 (41.7%) of the pump twins and live birth of a healthy infant in the remaining seven pregnancies.

The aim of this study was to report our experience with interstitial laser therapy in the first trimester of pregnancy complicated by TRAP sequence.

METHODS

This was a retrospective cohort study of all consecutive monochorionic diamniotic twin pregnancies with TRAP sequence, that underwent interstitial laser treatment at ≤ 14 + 3 weeks' gestation at our center, between January 2014 and April 2016; before commencement of the randomized TRAP Intervention Study (TRAPIST) in May 2016 (ClinicalTrials.gov: NCT02621645). The diagnosis of TRAP was confirmed in all cases by demonstrating the retrograde perfusion from the pump twin to the acardiac twin using color flow Doppler. Crown–rump length (CRL) of the pump twin and upper pole–rump length (URL) of the acardiac twin were measured, and (CRL − URL)/CRL ratio and URL/CRL ratio were calculated, as reported previously.

Interstitial laser treatment was performed under local anesthesia, with prophylactic maternal antibiotics and ultrasound guidance using an 18-gauge needle. A 400-nm Nd:YAG laser fiber (Dornier, Wessling, Germany) was introduced through the needle and placed close to the intra-abdominal part of the umbilical artery of the acardiac fetus. Coagulation was performed using a basic setting of 20–25 Watts. The procedure was considered successful when complete cessation of the reverse perfusion was confirmed on color flow Doppler. Women were discharged within 24–48 h after the procedure. Hospital records were reviewed to ascertain the pregnancy outcomes and neonatal mortality and morbidity.

RESULTS

During the study period, 12 pregnancies were diagnosed with TRAP and treated using IFL at a median gestational age of 13 + 5 (interquartile range (IQR), 13 + 4 to 14 + 0) weeks (Figure 1). The median CRL of the pump twin was 71.9 (IQR, 66.8–81.5) mm and the median URL of the acardiac twin was 44.3 (IQR, 41.4–55.8) mm. The (CRL − URL)/CRL ratio was 0.378 (IQR, 0.232–0.438) and the URL/CRL ratio was 0.620 (IQR, 0.563–0.765).

In all cases, one treatment was sufficient to achieve complete interruption of the perfusion of the acardiac twin with application of a median of 1480 (IQR, 980–2498) Joules. There were no procedure-related complications during or within 48 h after the intervention.
In one (8.3%) case, follow-up showed intrauterine death of the pump twin 14 days after intervention. All other cases (91.7%) resulted in a live birth at a median gestational age at delivery of 39 + 6 (IQR, 37 + 1 to 41 + 2) weeks (Figure 1). Median birth weight was 3370 (IQR, 2980–3480) g. There was no major neonatal morbidity or mortality. Preterm birth occurred in one case, at 32 + 0 weeks’ gestation.

**DISCUSSION**

This cohort study of monochorionic pregnancy with TRAP sequence demonstrates an overall survival rate of 92% and a high rate of live births at term when interstitial laser coagulation was performed prior to 14 + 3 weeks’ gestation. The findings of this study suggest that early intrafetal laser therapy does not increase fetal-loss rate in pregnancy with TRAP sequence, rather, it may be advantageous in comparison to waiting until a more advanced gestational age.

The spontaneous pregnancy-loss rate in the first trimester of TRAP pregnancy seems to be somewhere between 33% and 83%8,9. To date, there is no effective method to identify TRAP pregnancy at high risk of fetal demise, between the first and second trimester, as this is likely to occur acutely and unpredictably. In view of this high pregnancy-loss rate, elective intervention at an early pregnancy stage seems to be beneficial.

In contrast to this study, a previous study demonstrated a comparatively high fetal-loss rate of 42% after the procedure. The small sample size of both this study and that of Roethlisberger et al.10, limit comparative interpretation of the respective loss rates. However, it should be noted that in our population the median URL, as well as the (CRL – URL)/CRL and the URL/CRL ratios, showed a tendency towards bigger acardiac twins. The URL was 44.3 (IQR, 41.4–55.8) mm in our population vs 36.4 (IQR, 33.3–41.5) mm in the study of Roethlisberger et al.10. This is in contrast to their finding of a higher loss rate with increasing URL.

A limitation of this study is its retrospective design, which precludes definitive conclusions from being drawn regarding the superiority of first-trimester intervention in the absence of a matched control group. Hence, the TRAP Intervention Study (TRAPIST), a multicenter, open-label, randomized controlled trial, is expected to provide evidence for or against the benefit of early (12–14 weeks’ gestation) vs late (16–19 weeks) intervention in such pregnancy. In the interest of evidence-based medicine, recruitment for this trial should be supported by fetal medicine specialists.

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