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Outcome following selective fetoscopic laser ablation for twin to twin transfusion syndrome: an 8 year national collaborative experience

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ABSTRACT

Objective: With the recognition of the role of fetoscopic laser ablation for twin to twin transfusion syndrome (TTTS), there is a requirement for auditable standards for this technically challenging and specialized treatment. The purpose of this study is to report on the perinatal and medium-term neurodevelopmental outcomes following an 8-year national single center experience in the management of TTTS using the selective fetoscopic laser ablation technique.

Study design: An audit of all cases of TTTS treated with selective laser ablation by a single national fetal medicine team was performed. Overall perinatal survival and medium-term neurodevelopmental outcomes were reported and correlated with gestational age at diagnosis, placental location, volume of amnio-reduction, Quintero staging and percentage inter-twin growth discordance. Procedure-related complications were recorded.

Results: The overall fetal survival for the first 105 consecutive cases of TTTS was 61% (128/210 fetuses). Dual survival occurred in 47% (49/105) of cases, and with a single survival rate of 28% (30/105), perinatal survival of least one infant was achieved in 75% (79/105) of cases. No correlation was found between any clinical or sonographic marker and perinatal outcome, although dual survival was noted to be significantly decreased with increasing Quintero stage ($p = 0.041$). Currently, 86% of survivors have been reported to have a normal medium-term neurological outcome.

Conclusion: Fetoscopic laser ablation is the established optimal treatment for severe twin to twin transfusion syndrome (TTTS). We report comparable short and medium-term outcomes following the selective fetoscopic technique comparing results from our national program with internationally published single-center outcomes, supporting the efficacy and safety of this treatment at our center.

Introduction

Twin to twin transfusion syndrome (TTTS) complicates approximately 5–15% of monochorionic twin pregnancies, and is associated with an approximate 90% mortality if left untreated [1–3]. Fetoscopic laser ablation is the established first-line therapy for severe TTTS, and an overall survival rate of approximately 75% may be expected adopting current techniques [4–8]. As survival outcomes improve with expanding treatment techniques, focus is turning to medium-term neurocognitive and cardiac outcomes [9–12]. The Irish national fetal laser program was established in 2006, comprising of a single fetal medicine team from two large tertiary referral centers, serving as a national tertiary referral service for all 19 obstetric units in the country. Our national birth rate is approximately 75,000, however not all units offer routine early pregnancy ultrasonography. In the event of suspected TTTS, referring units have direct access to a member of the laser team, and suspected cases are generally reviewed within 24 h of referral.

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Selective fetoscopic laser photocoagulation of placental vascular anastomoses has been carried out on the first 105 cases of twin to twin transfusion syndrome (TTTS) by this collaborative national team over the past 8 years. Given the necessity for auditable standards, the purpose of this review is to establish firstly the perinatal survival outcomes and any procedure-related complications following selective fetoscopic laser ablation [13,14]. Secondly, we aim to report on the medium-term neurodevelopmental outcomes for this study population, and to compare these outcomes with other single-center international experiences.

Materials and methods

We performed an audit of all cases of TTTS in which fetoscopic laser ablation was performed over the past 8 years (2006–2014). Cases were identified within a Prenatal Diagnosis Registry. For each case, prior to treatment, a comprehensive fetal medicine review was undertaken including confirmation of chorionicity, detailed anatomical survey, placental assessment, and assessment of cardiac functional status. All cases suitable for inclusion in this review were diagnosed using standard ultrasonographic features of TTTS and categorized according to Quintero Stage [6]. In all cases, selective fetoscopic laser ablation was the intended primary procedure.

Prior to fetoscopic laser ablation all patients received written informed consent which included a comprehensive discussion regarding expected survival outcomes. Thirty cases were performed under local anesthesia, and seventy-five cases were performed under regional anesthesia. Peri-operative antibiotics and tocolysis were administered as per protocol. Selective fetoscopic laser treatment of placental vascular anastomoses was undertaken by a single team of three collaborative fetal medicine specialists. For each case the surgical team comprised of the primary operator and a second fetal medicine specialist, in addition to a sonography assistant and fetal medicine fellow. All procedures were performed in a similar fashion: a 10 or 12 French Cook Check-Flo Performer introducer sheath was introduced into the recipient sac under continuous ultrasound guidance. For cases with a posterior placenta a 2 mm Karl Storz 0° fetoscope was used, and in cases of an anterior placenta a 30° Albarran scope was chosen. After visualizing the vascular equator in its entirety, and following a consensus regarding all potential anastomoses, sequential photocoagulation of anastomoses using a neodymium:YAG laser was performed. A comprehensive review of all coagulated vessels ensured any anastomoses were re-examined and coagulated before an amnio-reduction completed the procedure. A karyotype was also routinely sent following patient consent. Fetal survival was confirmed within 24 h of the procedure. All mothers were reviewed for any immediate procedure-related complications prior to discharge. Follow-up for survivors included serial biometry, assessment for recurrent TTTS, and targeted fetal and neonatal echocardiography with an affiliated consultant fetal cardiologist.

The main outcome variable reported was perinatal survival, defined by neonatal survival to 28 days of life. Additional outcome variables included pre-operative details, operative details and post-procedural antenatal complications such as rates of pre-labor premature rupture of membranes (PPROM). In addition, the percentage pre-procedure inter-twin growth discordance was documented for all cases, following review of individual biometry data within an integrated ultrasound reporting database (Viewpoint®). Medium-term neurodevelopmental outcomes (greater than 6 months of age) were obtained by individual patient correspondence and pediatric review.

Descriptive variables are reported as medians with ranges. Continuous variables were analyzed using t test and Mann Whitney test. Fisher's exact test was used for categorical variables. With regards to ethical approval patients provided verbal and written consent at the time of the procedure for use of their details for research purposes at a later stage. Verbal communication by a member of the fetal medicine team was also part of standard follow-up care. For analysis purposes for this study all data was anonymised and data handling conformed to standard ethical requirements.

Results

A total of 106 cases of TTTS were scheduled for fetoscopic laser ablation between March 2006 and September 2014. Based on the Quintero staging system, this cohort included Stage 1, 9/106 (8%); Stage 2, 42/106 (40%); Stage 3 50/106 (47%); and Stage 4 5/106 (5%). There was one case of mono-amniotic twins and two cases of triplets with a mono-chorionic pair included in this study. Mean gestational age at diagnosis of TTTS was 19 + 4 weeks' (range 15 + 6/7–24 + 6/7), with a mean gestational age at laser of 20 + 1/7 (range 16 + 1/7–25 + 4/7). The mean percentage inter-twin growth discordance was 24% (range 1–51%), with 40% of cases having a growth discordance of greater than 20% prior to procedure. A posterior placenta was reported in 63 of 105 cases (60%). An average of 5.6 anastomoses was coagulated at each procedure. In all cases an amnio-reduction was performed to complete the procedure, with a mean volume of 2090 ml (range 600–4000).

In three cases, the laser photocoagulation procedure was considered to have been incomplete, whereby intra-operative hemorrhage necessitated the procedure to be abandoned before completion, and an amnio-reduction was then performed. In two cases a repeat fetoscopic laser ablation was performed, resulting in recipient survival in one case, and in the other case the second procedure was further complicated by chorio-amnionitis, which ultimately required pregnancy termination via hysterotomy. In one further case of severe morbid maternal obesity fetoscopy could not be attempted as the patient developed respiratory arrest on the operating table, and a perimortem hysterotomy was required before the procedure began. Therefore survival outcomes are reported on a total of 105 cases treated with selective fetoscopic laser ablation.

Overall fetal survival was 61% (128/210 fetuses). Dual demise occurred in 25% of cases (26/105 pregnancies). In 28% of cases (30/105), single fetal survival occurred. At least one survivor was noted in 75% (79/105) of cases. In one case of dual demise a karyotype confirmed a diagnosis of Turner syndrome. Perinatal outcomes, both in the overall population and categorized by Quintero stage, are presented in Table 1. Table 2 summarizes recently reported survival outcomes from single center fetoscopic laser programs, and are compared with our center's results.

The overall PPROM rate occurring within four weeks of the procedure was 10% (10/105). Additional complications such as persistent TTTS and twin anemia polycythemia sequence (TAPS) complicated a further 4 sets of twins. Dual survival was achieved in 2 of these 4 cases (one case each of TTTS and TAPS). For the overall study population, the mean gestational age at delivery was 29 + 5/7 weeks (range 17 + 1/7–40 + 2/7). For all survivors the mean gestational age at delivery was 32 + 1/7 weeks (range 24 + 2/7–40 + 2/7), and a total of 19% of cases delivered less than 28 weeks' gestation. The mean number of days gained from the time of procedure until time of delivery, overall, was 79 days (range 1–152).

Analysis of predictors of outcomes following fetoscopic laser ablation for TTTS, revealed no association between placental location ($p = 0.2219$), gestational age at diagnosis ($p = 0.2026$), volume of amnio-reduction ($p = 0.6701$) or increasing inter-twin-growth discordance ($p = 0.4647$) and any rate of fetal survival. Logistic regression analyses were performed for Quintero stage and survival, which revealed that dual survival was significantly decreased with increasing Quintero stage ($p = 0.041$). There were