

Outcomes after Laser Ablation in Twin-to-twin Transfusion Syndrome

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Abstract

Aim

Twin-to-Twin Transfusion Syndrome (TTTS) is associated with high perinatal morbidity and mortality in monochorionic twins. Ultrasound Doppler studies of the umbilical arteries (UAD) have a vital role in fetal assessment in multiple pregnancies complicated by TTTS. The Quintero staging is used to grade the severity of the condition.

Methods

The aim of the study was to describe UAD findings and outcomes in a cohort of 78 twin pregnancies treated with laser ablation.

Results

Of the 78 twin pregnancies, 39 women had two surviving babies (50%) and 17 (22%) had a single survivor. The most frequent Quintero stage at diagnosis was Stage three (38%, 30/78), followed by Stage two (32%, 25/78), Stage one (24%, 19/78) and Stage four (5%, 4/78). The Quintero stage was not significantly associated with survival (chi sq 5.31 p=0.151).

While 50% of pregnancies had normal UAD at the time of TTTS diagnosis, 50% had at least one abnormal UAD. A normal UAD was not associated with higher survival (68% v 53%, chi sq 3.26 p=0.071).

Conclusion

Laser ablation for TTTS was associated with 50% double survival and 22% single survival. UAD abnormalities or the Quintero stage was not associated with survival after laser ablation.

Introduction

Twin-to-Twin Transfusion Syndrome (TTTS) is associated with high perinatal morbidity and mortality in monochorionic twins. It is associated with an increased risk of fetal loss and spontaneous and iatrogenic preterm delivery ¹. In TTTS the donor twin can become growth restricted and anaemic while the recipient twin grows discordantly larger and develops polycythemia.

Ultrasound Doppler studies of the umbilical arteries (UAD) have a vital role in fetal assessment in multiple pregnancies by screening and diagnosing common complications such as uteroplacental insufficiency, fetal anemia and growth restriction². Ultrasound examination also has a crucial role in the assessment of multiple pregnancies at high risk of TTTS. The Quintero method is commonly used for staging TTTS by utilizing the presence or absence of donor bladder filling, abnormal fetal UAD and other Doppler measurements, fetal hydrops and fetal demise.

Other ultrasound features described in TTTS include growth discordance between the two twins (>20% of fetal size difference) and folding of inter-twin membrane may appear as an early sign of TTTS due to disparity in amniotic fluid volumes in two sacs.⁴ In early pregnancy, there may be a difference in nuchal translucency between the twins or a significant difference in umbilical cord diameter. The recipient twin is usually larger in size with an increased estimated fetal weight (EFW), polyhydramnios, large urinary bladder, evidence of fetal hydrops and fetal cardiomegaly. In certain cases, fetal echocardiography may also show aorto-ventricular valve incompetence. The donor twin on the other hand is the small twin (with decreased weight), can appear "pinned" to the side of the gestational sac, may show evidence of fetal anemia, small or absent urinary bladder and oligohydramnios^{2,3}.

While a number of treatments for this condition have been suggested in the past including serial amniocentesis, septostomy and fetoscopic laser ablation, it is now clear that laser ablation is the optimal method of treatment, with a success rate of 49% for double fetal survival and 39% for single fetal survival⁵.

The predictors of success or failure of laser ablation are not clear. This audit was undertaken to review results of TTTS treated with laser ablation and identify any characteristics, especially UAD parameters, that can predict which procedures are likely to be successful.

Methods

The aim of the study was to describe UAD findings in a cohort of TTTS patients treated with laser ablation. In addition, the clinical outcomes from laser treatment of TTTS in patients treated at the Rotunda Hospital, Dublin between 2006 and 2016 were recorded. The Rotunda Hospital is a large tertiary care centre with approximately 8,500 to 9,000 deliveries a year.

A retrospective cohort study of cases of multiple pregnancies complicated by TTTS who were subsequently treated with laser ablation in a single tertiary maternity hospital was conducted. There is a dedicated multiple birth clinic, fetal assessment unit and laser treatment services for TTTS. All cases treated for TTTS with laser ablation in the period from 2006 to 2016 were included. All cases of TTTS were managed under the supervision of single lead fetal medicine specialist with two more fetal medicine specialists and two fetal medicine fellows. The same technique for laser ablation was used in all cases: a 10 or 12 French Cook Check-Flo Performer introducer sheath is introduced into the recipient sac under continuous ultrasound guidance transabdominally. For cases with a posterior placenta a 2mm straight Karl Storz fetoscope was used, and a 2mm curved Karl Storz fetoscope for anterior placentae. After visualizing the whole vascular equator, all potential anastomoses are recognised and photocoagulated using a neodymium:YAG laser, using a Solomon technique.

An amnioreduction is then performed at the completion of each procedure. All patients are followed up by ultrasound on the next day, and then weekly, to check fetal wellbeing.

Data on gestation and stage of TTTS at diagnosis, UAD patterns, Quintero stage, the gestation at laser ablation treatment, the gestation at delivery, and any iatrogenic complications that may have occurred were collected. The main parameter of interest in this study was the prevalence of UAD abnormalities in cases of TTTS prior to treatment with laser, and the subsequent neonatal outcomes.

Data were collated using an Excel spreadsheet. Statistical analysis was performed using IBM SPSS Statistics Version 24. Ethical approval was obtained from the hospital research and ethics committee.

Results

Over a 10-year period there were 93 patients who underwent selective fetoscopic laser ablation treatment for TTTS. Overall, 82 women delivered in the Rotunda hospital and they are described here. The mean (range) maternal age was 31 years (17 to 42 years). The mean (range) gestational age at diagnosis of TTTS was 19+3 weeks (15+4 to 24+6 weeks).

The mean (range) gestational age at laser treatment was 19+6 weeks (15+6 to 24+6 weeks), giving a mean diagnosis-to-treatment interval of 3 days. The procedure was performed under regional anesthesia in 68% of cases (63/93) or local anesthesia in 33% of cases (30/93). Out of the total of 93 sets of multiple pregnancy, there were 4 sets of triplets, two cases of failed treatment due to excessive bleeding and 9 cases did not deliver in the same tertiary unit.

Of the 82 women who delivered in the Rotunda hospital, 78 were twin pregnancies and there were 4 triplet pregnancies. Of the triplet pregnancies, one resulted in the delivery of three live neonates, two resulted the delivery of two live neonates, and one resulted in the loss of all three fetuses.

The following results focus on the remaining 78 cases of twin pregnancies. Of the 78 twin pregnancies, 39 women had 2 surviving babies (50%) and 17 (22%) had a single survivor (fig1).

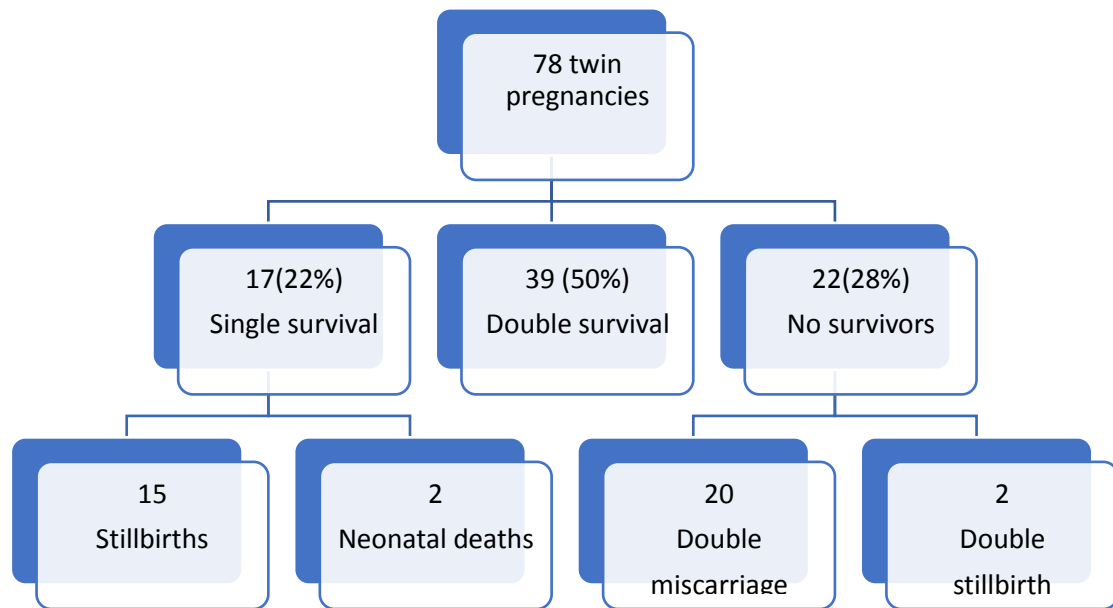
The most frequent Quintero stage at diagnosis was Stage three (38%, 30/78), followed by Stage two (32%, 25/78), Stage one (24%, 19/78) and Stage four (5%, 4/78). The Quintero stage was not significantly associated with survival (chi sq 5.31 p=0.151).

While 50% of pregnancies had normal UAD at the time of TTTS diagnosis, 50% had at least one abnormal UAD finding. Of the abnormal UAD, absent end diastolic flow in the donor twin (AEDF) was the most common (37%, 29/78), AEDF in the recipient 2% (2/78), reversed end diastolic flow (REDF) in donor twin was 6% (5/78), while 4% (3/78) had a raised SD ratio (Table 1). The association of the Quintero stage and abnormal Doppler waveforms is detailed in table 1 and figure 2.

The fetal survival rate with a normal UAD was 53/78 (68%) and with any UAD abnormality was 42/78 (53%). A normal UAD was not associated with survival (chi sq 3.26 p=0.071) (Table 2).

Most commonly, the placenta was located posteriorly (60% cases), versus 36% anterior and 4% fundal.

Figure 1: The neonatal outcome of 78 twin pregnancies with TTTS treated with laser ablation.



Of the 56 women with liveborn deliveries, 47 were delivered by caesarean section, 13(16%) had dual vaginal deliveries, and there were two cases of vaginal delivery for twin 1 followed by emergency Caesarean section for twin 2. The mean (range) gestational age at delivery was 30+1 weeks (23+3 to 40+3 weeks). This gives a mean laser-to-delivery interval of 10+2 weeks.

Table 1: The correlation of abnormal umbilical artery Doppler findings and Quintero stage in 78 sets of twins.

	Number (%)78	Quintero Stage 1 N =19	Quintero Stage 2 N=25	Quintero stage 3 N=30	Quintero stage 4 N=4	Mean Gestational Age (weeks)
Normal Doppler	39/78 (50%)	11/19	20/25	8/30	0/4	19.6
Total Abnormal Dopplers	39/78 (50%)	8/19	5/25	22/30	4/4	
AEDF Donor	29	7	2	20	0	21
AEDF Recipient	2	1	0	1	0	22.1
REDF Donor	5	0	0	1	4	19.3
Raised SD	3	0	3	0	0	21.1

Figure 2
Umbilical Doppler abnormalities related to Quintero stage in 78 twin pregnancies that underwent laser ablation for TTTS

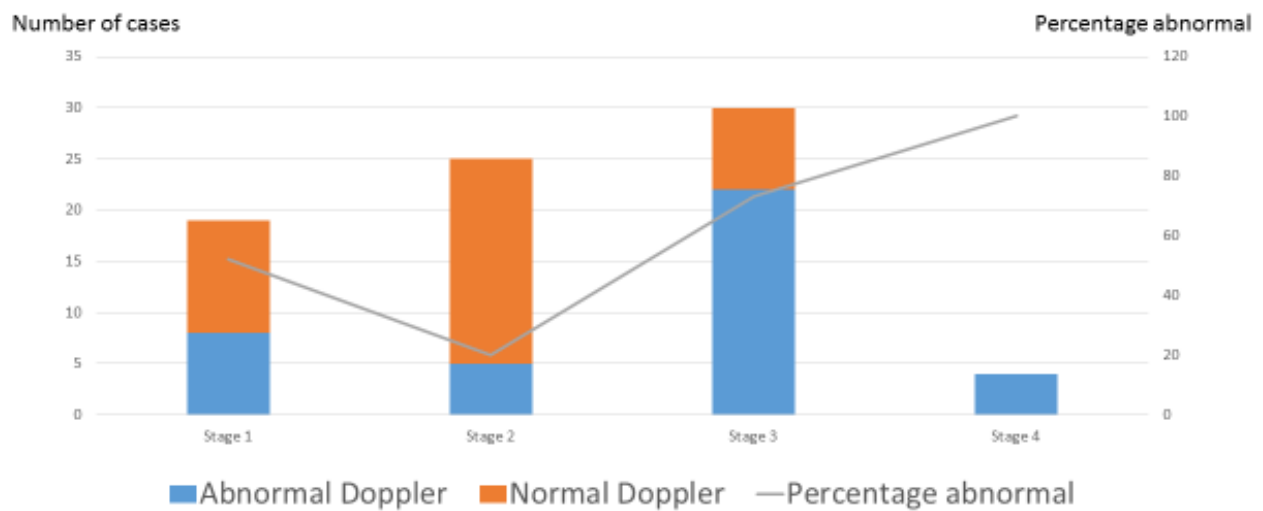


Figure 2: Umbilical Artery Doppler abnormalities related to Quintero stage in 78 twin pregnancies that underwent laser ablation for TTTS.

Table 2: Survival of 1⁵⁶ babies who underwent laser ablation for TTTS in different Quintero stages and in relation to the umbilical artery Doppler analysis.

	Double survival Number babies Survived	Single survival Number babies survived	Double loss Number babies died	Total survival Number babies (%)
Quintero Stage 1 N=38	20/38	3/38	12/38	23/38(60%)
Quintero Stage 2 N=50	32/50	4/50	10/50	36/50 (72%)
Quintero Stage 3 N=60	24/60	9/60	18/60	33/60 (55%)
Quintero Stage4 N=8	2/8	1/8	4/8	3/8 (37%)
Total normal Doppler analysis N=78	48/78	5/78	20/78	53/78(68%)
Total abnormal Doppler analysis N=78	30/78	12/78	24/78	42/78(53%)
AEDF donor N=58	26/58	8/58	16/58	34/58(58%)
AEDF recipient N=4	2/4	1/4	0/4	3/4(75%)
REDF donor N=10	2/10	1/10	6/10	3/10(30%)
Abnormal SD ratio N=6	0/6	2/6	2/6	2/6(33%)

AEDF = absent end diastolic flow, REDF = reversed end diastolic flow, SD ratio = systolic diastolic ratio

Discussion

In this study, abnormal UAD findings and perinatal outcomes of TTTS over 10 years treated with selective fetoscopic laser ablation supervised by a single lead fetal medicine specialist were evaluated. As outlined above, UAD was abnormal at diagnosis in 50% of the cases with the commonest abnormality being absent end diastolic flow in the donor fetus. We were unable to identify any correlation between Quintero stage or UAD abnormalities and overall survival. In this study, double survival was 50%, single survival was 22% and double miscarriage was 28%. Only 7% delivered after 36 weeks of gestation. In this study survival of babies with TTTS who have normal Doppler studies is 68%, but this drops to 53% when there is any Doppler abnormality, although this difference was not statistically significant. Doppler abnormalities were associated with Quintero stages three and four. This is not surprising as stage three diagnostic criteria is dependent on the findings of abnormal Doppler studies, but these abnormalities are not exclusively in the umbilical artery and can be found in the ductus venosus or umbilical vein Doppler parameters. Survival decreased with the advancing Quintero stage; 60% in stage one, 72% in stage two, 55% in stage three and 37% in stage 4. Another study conducted in Florida showed double survival of 49% with single survival of 39%. Our survival rates are comparable to international rates.⁵ One randomized controlled trial showed that fetal survival was significantly lower in Quintero stage three cases compared with stage one and two. This study shows a reduction in survival in stage three cases with a further reduction in stage four cases⁶. This study can be helpful in counselling of women with TTTS at different Quintero stages as survival with abnormal Dopplers is worse in stage three and four compared to stage one and two. Although not statistically significant, the reduced survival in groups 3 and 4 was similar to the published literature.

It is notable that two cases had failed TTTS due to excessive bleeding at the time of procedure and were excluded. We excluded those cases who were referred to other centres for delivery on maternal request as well.

It is important to note that the number of cases treated progressively increased every year with one case being treated in 2006 and 16 cases treated in 2016. This is possibly attributed to greater awareness in monitoring of multiple pregnancies at referral hospitals. General application of early booking scans and serial scanning allows accurate gestational assessment, determination of chorionicity, early detection of TTTS and referral to tertiary care for management.

Declaration of Conflicts of Interest:

All of the authors have no conflict of interest.

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