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Doppler Finding, Cardiovascular Function Assessment, and Fetuses' Survival Following the Fetoscopic Laser in Twin-to-Twin Transfusion Syndrome

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Abstract

Introduction: This study aimed to evaluate the effectiveness of selective laser photocoagulation of communicating vessels (SLPCV) on cardiac function in twins with twin-to-twin transfusion syndrome (TTTS).

Methods: This retrospective cohort study evaluated 178 women with twin pregnancies complicated with TTTS and scheduled for SLPCV between 16 and 26 weeks of gestation. The severity of TTTS was determined by Quintero staging and the severity of cardiovascular disorders by the CHOP (Children's Hospital of Philadelphia) score. Patient survival was evaluated through a one-month-after-birth follow-up of fetuses.

Results: The study revealed significant improvements in Doppler indices in both donors and recipients after SLPCV. The CHOP score also significantly decreased after the intervention. One-month-after-birth survival rates were 55.1% in donors and 56.7% in recipients. Some Doppler indexes of fetuses before SLPCV could predict survival until one month after birth.

Conclusion: The study suggests that SLPCV can improve cardiac function in fetuses with TTTS and that some Doppler indexes can predict survival outcomes. Additionally, the severity of TTTS can be a powerful indicator of the severity of cardiovascular complications.

Keywords: CHOP score; Twin-to-twin transfusion syndrome; Laser photocoagulation; Fetal surgery.

Introduction

Twin-to-twin transfusion syndrome (TTTS) is a severe pathological complication affecting about 10% to 15% of monochorionic twin pregnancies and is the result of unbalanced vascular anastomosis of twin placental veins and arteries and the transfer of nutrients and blood from one to the other.[1] It is characterized by increasing the deepest vertical pocket (DVP) of amniotic fluid higher than 8cm in the amniotic sac of the recipient twin along with decreasing this marker lower than 2 cm in the donor twin.[2,3] There are a variety of predisposing factors as regards the occurrence of such a complication, which can be mentioned as structural defects in the vasculature bed, disqualification of anastomoses, and chronicity of transfusion.[4]

Due to severe imbalance in perfusion and therefore hemodynamic instability in both twins, in case of failure to treat, high perinatal mortality up to 90% can be expected frequently by reason of the occurrence of polycythemia and anemia, neonatal hypotension and hypertension, polyhydramnios and preterm rupture of membrane and preterm labor, asphyxia, and respiratory distress syndrome.[4] In this regard, current guidelines strongly recommend serial sonography beginning in the first trimester and every 2 weeks from 16 weeks of gestation until 26 weeks as screening in monochorionic diamniotic twin pregnancies for the early detection of TTTS.[5,6]

Ultrasound is the gold standard tool for the early detection of TTTS by tracking volume overload and polyuria followed by polyhydramnios in one twin and, paradoxically, oliguria followed by oligohydramnios in another twin.[7] For staging the severity of this phenomenon, the assessment of arterial and venous Doppler patterns along with bladder filling is very helpful.[8] Nowadays, selective laser photocoagulation of communicating vessels

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(SLPCV) between twins is the selective therapeutic option for TTTS with high successfulness, maintaining the long-term survival of infants.[9] According to the literature, this treatment approach could lead to long-term survival of up to 65% in both fetuses and up to 88% in a single fetus.[10] In other words, despite proper treatment and due to the occurrence of some neurological and cardiovascular sequels, we will continue to see infant mortality, especially in the long term.[11,12]

One of the most important complications related to TTTS caused by hemodynamic disorder and vascular load inconsistency is heart complications in newborns. In fact, acute and chronic fetal cardiovascular impacts of TTTS cannot be hidden. Comprehensive studies on cardiovascular complications of this phenomenon are being conducted. It has been demonstrated that increasing umbilical venous flow can lead to elevating preload followed by an increasing stretch of the cardiac chamber, releasing natriuretic peptides and thus triggering dieresis and polyhydramnios.[13] Moreover, the secretion of endothelin as a vasoconstrictor can lead to hypertension which may result in cardiac hypertrophy and valvular defects.[14] Besides, in donor twins suffering from TTTS, hypovolemia can lead to oligohydramnios followed by the activation of the renin-angiotensin pathway leading to hypertension and thus cardiomyopathy.[6] The set of these pathophysiological changes can lead to mortality and morbidity caused by cardiovascular and Doppler disorders in these patients. Therefore, it is very necessary to evaluate cardiovascular and Doppler abnormalities in these cases, especially in the long term and after applying treatment to preserve their survival. The CHOP score (Children's Hospital of Philadelphia) is a scoring system that demonstrates the cardiovascular state of the twins with TTTS and is measured by a peripheral Doppler and some intra-cardiac echocardiographic parameters of cardiac function.[15]

A recent survey shows the role of a fetal Doppler before a laser in the survival of two fetuses and uses it as a predictive factor.[16] However, the role of the CHOP score in predicting the survival of fetuses is not clear and some studies represent it as a predictive factor, but others do not. The current study aimed to assess cardiac function by evaluating CHOP score changes and Doppler changes in donor and recipient fetuses after SLPCV due to TTTS. Furthermore, it assessed the prediction of the value of Doppler indexes and the CHOP cardiovascular score of fetuses before SLPCV on the survival of fetuses.

Materials and Methods

Study Population

This retrospective cohort study took place at Shariati Hospital, which is affiliated with Tehran University of Medical Sciences in Tehran, Iran. The study was conducted from October 2018 to September 2022 and involved women who had twin pregnancies complicated by TTTS. These women were scheduled to undergo SLPCV between 16 and 26 weeks of gestation. Since the establishment of the fetoscopic laser photocoagulation (FLP) center at Shariati hospital in Tehran, all cases of TTTS have been referred to this center. As the only active FLP center in Iran, it has been responsible for managing TTTS cases throughout the country.

The inclusion criteria consisted of all women with TTTS monochorionic diamniotic twin pregnancies that were treated with FLP.TTTS was defined as the presence of DVP ≥ 10 cm after 20 weeks or ≥ 8 cm before 20 weeks along with a distended bladder in the recipient twin and the presence of oligohydramnios with DVP ≤ 2 cm with a small bladder.[17] In this regard, those fetuses with any other malformations, amniocentesis before the procedure, or evidence of premature rupture of membranes before operation were all excluded from the study.

Study Measurements

The Fetal Laser FLP procedure involved the administration of regional or local anesthesia. It began with a small incision in the skin, followed by the percutaneous insertion of a trocar into the amniotic cavity. Ultrasonography was used to guide the insertion process, employing the 'Seldinger' technique. Subsequently, a 3.3-mm fetoscope (specifically the Karl Storz model 11506AA from Germany) was introduced into the amniotic cavity of the recipient. In cases where the placenta was located at the anterior of the uterus (known as the anterior placenta), a fetoscope equipped with a curved trocar was utilized. All the communicating intertwine placental anastomoses, including arteriovenous (AV), arterioarterial (AA), and venovenous (VV), were coagulated using a diode laser with a 400-600-micron laser fiber. At the conclusion of fetoscopic laser coagulation, the amniotic fluid was drained through the sheath until a normal amount of amniotic fluid (the maximum vertical pocket ≤ 6 cm) was confirmed.

All the patients received the same post-operative care and monitoring in the postnatal ward. After follow-up sonography was conducted 24 hours later, women who did not have any complications were discharged. Another follow-up sonography was conducted two weeks later to check for complications and the recurrence of TTTS. It was recommended that all women schedule regular visits with a perinatologist every two weeks until the end of their pregnancy.

Baseline characteristics including mothers' age, gestational age, and fetal weight were assessed and entered into the checklist. Pre- and post-procedural ultrasonographic and echocardiographic scans were obtained by an experienced perinatologist and pediatric cardiologist. Before the assessment, all women were informed about TTTS and its therapeutic approaches

as well as the safety of ultrasonography and fetal echocardiography. The ultrasonic parameters assessed before and after the procedure included the evidence of polyhydramnios, the value of DVP, selective intrauterine growth restriction (SIUGR) and its classification, placenta orientation, intrauterine fetal death (IUFD), umbilical artery flow velocity waveforms indices (umbilical arterial systolic/diastolic [S/D] ratio, pulsatility index [PI], absence of end-diastolic velocities [AEDV], reversed end-diastolic velocities [REDV]), middle cerebral artery (MCA) parameters (the peak systolic velocity [PSV], PI), and vascular parameters of ductus venosus (PI, AEDV, REDV). Also, the neonatal dimensions including cervical length, the need for the cerclage, and survival status of the fetuses 24 hours after the laser, one week after the laser, at birth, and one month after birth were assessed. The severity of TTTS was determined using the TTTS Quintero staging and based on ultrasonography findings as stage 1 (Polyhydramnios–oligohydramnios sequence: DVP > 8 cm in the recipient twin and DVP < 2 cm in the donor twin, bladder of the donor twin still visible), stage 2 (bladder of the donor twin no longer visible, no critical abnormal Doppler), stage 3 (critical abnormal Doppler waveforms), stage 4 (the presence of hydrops) and stage 5 (demise of one twin or both twins).[18]

The cardiovascular state of the fetus was also classified using the CHOP scoring system which includes the presence of cardiovascular abnormal parameters including ventricular hypertrophy, cardiomegaly, ventricular systolic function, mitral valve regurgitation, tricuspid valve regurgitation, mitral valve E/A ratio, tricuspid valve E/A ratio, ductus venosus, pulsatile umbilical vein, pulmonary regurgitation, right ventricular outflow tract (that all are measured in recipient), and end-diastolic flow of the umbilical artery (that is measured only in donor).[15] The CHOP score ranged from 0 to 20 and was classified as stage 1 (score ranging from 0 to 5), stage 2 (score ranging from 6 to 10), stage 3 (score ranging from 11 to 15), and stage 4 (score ranging from 16 to 20). A higher CHOP score indicates a worse heart condition. If the cervical length was equal to or shorter than 15-mm, cerclage was done for the patient.

Statistical Analysis

The statistical analysis for this study was performed using IBM SPSS Statistics version 23.0 for Windows (IBM, Armonk, New York). Prior to analysis, the normality of the data was assessed. Numeric variables with a normal distribution were presented as mean ± standard deviation (SD), while non-normal data were represented as median (interquartile range, IQR). Qualitative data were reported as frequency (%). To compare quantitative variables between the groups, a t-test was employed for normally distributed data, and the Mann-Whitney test was used for non-normally distributed data. Categorical variables were analyzed using either the chi-square test or Fisher's exact test. The significance level was set at $P < 0.05$.

Results

In total, 178 women with twin pregnancies complicated with TTTS and scheduled for SLPCV were included in the study. The baseline characteristics of the study subjects are summarized in Table 1. Concerning Quintero classification, 3.3% of the participants were classified as stage I, 34.3% of them were classified as stage II, 56.7% of them were classified as stage III, and 5.6% of them were classified as stage IV.

Ultrasonic Doppler findings in donor and recipient

Table 1. Baseline Characteristics of the Study Population

Characteristics	Value
Mean age of mother, year	29.72 ± 5.53
Mother weight, kg	71.34 ± 11.51
Mother height, cm	161.40 ± 6.86
Mother body mass index, kg/m^2	26.74 ± 4.22
Preoperative cervical length, cm	32.63 ± 6.69
Mean total number of anastomoses, median (IQR)	36.0 (24-46)
Gestational age at diagnosis, day	142.22 ± 15.36
Gestational age at diagnosis, week	20.31 ± 2.19
Gestational age at intervention time, day	145.04 ± 15.46
Gestational age at intervention time, week	20.72 ± 2.2
Inter-twin estimated fetal weight discordance, %	28.0 (18-38)
Recipient twin fetal weight, gram, median (IQR)	339.5 (276.2-480.2)
Donor twin fetal weight, gram, median (IQR)	239.0 (193.5-326.5)
Prevalence of polyhydramnios, %	162 (91.0)
Prevalence of SIUGR, %	104 (58.4)
SIUGR classification, %	
I	34 (19.1)
II	67 (37.6)
III	4 (2.2)
Anterior placenta orientation, %	75 (42.1)
Cerclage, %	28 (15.7)
The time of cerclage, %	
Before fetal intervention	12 (6.7)
During fetal intervention	12 (6.7)
After fetal intervention	4 (2.3)
Maximum vertical pocket, cm (recipient)	10.68 ± 3.02
Maximum vertical pocket, cm (donor)	1.11 ± 0.42
Quintero classification, %	
I	6 (3.3)
II	61 (34.3)
III	101 (56.7)
IV	10 (5.6)

Abbreviations: SIUGR, selective intra uterine growth retardation; IQR, interquartile range.
Data are presented as mean (±SD, range) or n (%) or median (IQR).

fetuses before and after interventions are indicated in Table 2. As compared to the initial assessment of Doppler markers, in both donors and recipients, a significant improvement in Doppler indices including umbilical artery S/D, umbilical artery PI, umbilical artery, AEDV and/or REDV, MCA PSV, MCA PI, MCA resistance index, ductus venosus PI, and ductus venosus AEDV and/or REDV was revealed after the intervention. Also, the CHOP score reduced 48 hours after the intervention and significantly reduced 8 weeks after the intervention ($P<0.001$).

The usage of a repeated measures ANOVA with a Greenhouse-Geisser correction demonstrated a significant difference in chop scores before and after the interventions ($F=621.657$, $P<0.001$). Further examination through post hoc tests utilizing the Bonferroni correction indicated that, on average, the chop score decreased by 1.24 after 48 hours ($P<0.001$) and subsequently decreased by an additional 1.85 between the 48-hour and 8-week marks ($P<0.001$).

As shown in Table 3 and regarding the overall survival of the patients after the intervention, one-month-after-birth survival rates were 55.1% in the donors and 56.7% in the recipients (Figure 1). We reported just one fetus survived, at least one fetus survived (one or two fetuses), and two fetuses survived 24 hours after the laser, at birth, and one month after birth (Table 4).

Of baseline Doppler parameters assessed in the fetuses (Table 5), increased mid-cerebral artery PSV in the donor and higher ductus venosus PI in the recipient could effectively predict IUFD in donor patients with TTTS undergoing SLPCV. Also, the main determinants of intrauterine death in the recipients were increased umbilical artery PI and mid-cerebral artery PSV in donors (Table 6). According to the multivariable linear regression analysis with the presence of baseline parameters (Table 7), the changes in the CHOP score following the intervention could be predicted by lowering the Quintero score (beta = -0.156, $P=0.042$). The mean difference in the CHOP score after the intervention as compared to before that in survived and non-survived donor subgroups was 0.17 ± 0.46 and 0.33 ± 0.49 respectively, indicating no difference ($P=0.283$). Similarly, the two survived and non-survived recipient subgroups had a

Table 2. Ultrasonic Findings (Doppler and CHOP Score) in Donor and Recipient Fetuses Before and After SLPCV

Parameter	Before Intervention	After Intervention	*P* Value
Umbilical artery S/D (donor)	4.6 (3.5-6.2)	4.4 (3.4-5.6)	<0.001
Umbilical artery PI (donor)	1.5 (1.3-1.8)	1.4 (1.2-1.7)	<0.001
Umbilical artery AEDV/REDV (donor)	93 (52.2)	---	
MCA PSV (donor)	25.5 (21.0-31.4)	24.3(19.8-29.2)	<0.001
MCA PI (donor)	1.7 (1.4-2.1)	1.6 (1.5-1.8)	<0.001
MCA RI (donor)	0.8 (0.7-0.9)	0.4 (0.3-0.5)	<0.001
MCA S/D (donor)	4.2 (3.5-5.4)	3.1 (3.2-4.6)	<0.001
MVP (donor)	3.5 (2.4-4.9)	2.7 (1.6-3.8)	<0.001
DV PI (donor)	1.1 (0.7-1.6)	1.0 (0.5-1.4)	<0.001
DV AEDV/REDV (donor)	6 (3.4)	---	
Velocity (donor)	26.3 (20.2-31.5)	24.1 (18.6-27.8)	<0.001
Umbilical artery S/D (recipient)	4.0 (3.4-5.1)	3.8 (3.3-4.9)	<0.001
Umbilical artery PI (recipient)	1.4 (1.2-1.7)	1.3 (1.2-1.6)	<0.001
Umbilical artery AEDV/REDV (recipient)	9 (5.1)	---	
MCA PSV (recipient)	27.1 (22.4-32.4)	26.3 (21.3-30.6)	<0.001
MCA PI (recipient)	1.5 (1.3-1.8)	1.2 (1.0-1.5)	<0.001
MCA RI (recipient)	0.8 (0.7-0.9)	0.4 (0.3-0.6)	<0.001
MCA S/D (recipient)	4.5 (3.7-5.7)	3.7 (2.8-4.9)	<0.001
DV PI (recipient)	1.2 (1.0-1.4)	0.8 (0.7-1.0)	<0.001
DV AEDV/REDV (recipient)	6 (3.4)	---	
MVP (recipient)	6.3 (5.0-7.6)	4.3 (3.7-5.4)	<0.001
Velocity (recipient)	27.8 (24.0-35.1)	26.2 (22.3-32.6)	<0.001
CHOP score after 8 weeks, median (IQR)	5.0 (4-7)	2.0 (1-3.75)	<0.001
CHOP score after 48 hours, median (IQR)	5.0 (4-7)	4.0 (3-5)	<0.001

Abbreviations: SLPCV, selective laser photocoagulation of communicating vessels; S/D, systole/diastole; PI, pulsatility index; AEDV, absence of end-diastolic velocities; REDV, reversed end-diastolic velocities; MCA, middle cerebral artery; PSV, peak systolic velocity; RI, resistive index; MVP, mean vertical packet; DV, ductus venosus; CHOP, Children's Hospital of Philadelphia; ; IQR, interquartile range.
Data are presented as n (%) or median (IQR). The Mann-Whitney test and independent t-test were used to compare ultrasonic findings before and after SLPCV.

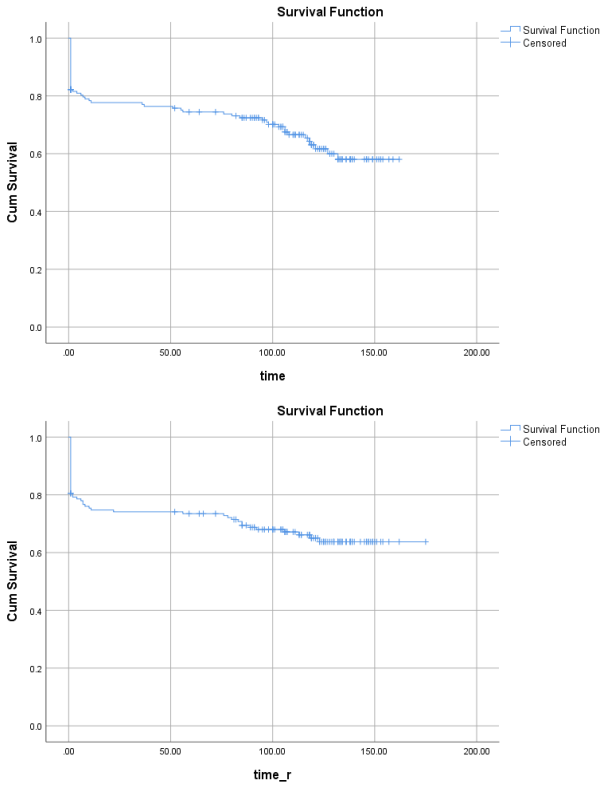

Figure 1. (A) Kaplan-Meier Curve of Fetal (Donor) Survival After the Fetoscopic Laser, (B) Kaplan-Meier Curve of Fetal (Recipient) Survival After the Fetoscopic Laser

mean difference in the CHOP score of 0.17 ± 0.45 and 0.33 ± 0.50 respectively, showing no difference ($P = 0.375$). The difference in the pre-laser CHOP score could not predict the intrauterine death or survival of donors and recipients.

Discussion

In our study, both donors and recipients revealed a significant improvement in Doppler indices after the intervention. Also, the CHOP cardiovascular score significantly reduced after the intervention. One-month-after-birth survival rates were 55.1% in the donors and 56.7% in the recipients. One-month-after-birth survival of at least one fetus was 79.1%, and two-fetus survival was 42.1%. Increased mid-cerebral artery PSV in the donor and higher Ductus Venosus PI in the recipient could effectively predict intrauterine death in donor patients with TTTS undergoing SLPCV. Also, the main determinants of intrauterine death in the recipients were increased umbilical artery PI and mid-cerebral artery PSV in donors. The difference in pre-laser CHOP score could not predict the intrauterine death or survival of donors and recipients. The changes in the CHOP score following the intervention could be predicted by lowering the Quintero score.

Both fetuses exhibited cardiac remodeling when double transfusion syndrome was diagnosed, but only the recipient showed significant diastolic dysfunction. Fetal therapy had a positive impact on most echocardiographic measures, although postnatal echocardiographic alterations continued to be present in both fetuses.[19] Despite the high frequency and intensity of prenatal cardiac overload in recipients, the majority of TTTS cases tend to resolve and return to normal after undergoing laser treatment. However, because of the increasing incidence of congenital heart disease and especially pulmonary stenosis, in-utero and postnatal monitoring is necessary.[20] Cardiovascular complications related to

Table 3. Post-procedural Outcome of Fetuses and Neonate

Survival Status (Donor)	No. (%)
24 hours after the laser	142 (79.8)
One week after the laser	126 (70.8)
At birth	106 (59.6)
One month (30 days) after birth	98 (55.1)
Survival status (recipient)	**No. (%)**
24 hours after the laser	145 (81.5)
One week after the laser	132 (74.1)
At birth	106 (59.6)
One month (30 days) after birth	101 (56.7)

Table 4. Post-procedural outcome of fetuses

	No Survived	Just One Survived	At Least One Survived (One or Two Fetuses)	Two Survived
24 Hours after the laser	15 (8.4)	40 (22.5)	163 (91.6)	123 (69.1)
At birth	29 (16.3)	46 (27.5)	128 (73.5)	82 (46)
One month (30 days) after birth	32 (18)	50 (28.1)	125 (70.2)	75 (42.1)

Data are presented as No. (%).

Table 5. The Doppler Index Predictor of Survival in Donor's Fetuses

Characteristics	Survived	Non-survived	*P* Value
Donor			
Umbilical artery S/D	4.7 (3.5-6.4)	4.6 (3.4-5.9)	0.770
Umbilical artery PI	1.5 (1.3-1.8)	1.5 (1.3-1.7)	0.807
Mid-cerebral artery PSV	26.6 (22.4-32.4)	24.8(19.9-29.7)	0.043
Mid-cerebral artery PI	1.7 (1.5-2.1)	1.7 (1.4-2.0)	0.120
Ductus Venosus PI	1.1 (0.7-.1.5)	1.2 (1.1-.1.6)	0.675
Recipient			
Umbilical artery S/D	3.9 (3.2-5.2)	4.2 (3.6-5.0)	0.400
Umbilical artery PI	1.4 (1.2-1.7)	1.5 (1.3-1.8)	0.535
Mid-cerebral artery PSV	27.8 (22.4-32.0)	28.4 (23.1-34.1)	0.672
Mid-cerebral artery PI	1.6 (1.4-1.8)	1.5 (1.3-1.8)	0.415
Ductus venosus PI	1.2 (1.0-1.4)	0.99 (0.7-1.2)	0.017

Abbreviations: S/D, systole/diastole; PI, pulsatility index; PSV, peak systolic velocity.
Data are presented as median (IQR). The Mann-Whitney test was used to compare the Doppler indexes between survived and non-survived fetuses

Table 6. The Doppler Index Predictor of Survival in Recipient's Fetuses

Characteristics	Survived	Non-survived	*P* Value
Donor			
Umbilical artery S/D	4.7 (3.4-7.0)	4.4 (3.5-5.7)	0.122
Umbilical artery PI	1.5 (1.3-1.8)	1.6 (1.4-1.9)	0.044
Mid-cerebral artery PSV	23.2 (19.1-29.4)	26.8 (22.5-32.5)	0.019
Mid-cerebral artery PI	1.7 (1.5-2.1)	1.6 (1.4-1.9)	0.158
Ductus venosus PI	1.1 (0.6-1.5)	1.2 (0.8-1.6)	0.670
Recipient			
Umbilical artery S/D	4.1 (3.5-5.1)	3.9 (3.4-5)	0.443
Umbilical artery PI	1.4 (1.2-1.7)	1.4 (1.3-1.8)	0.905
Mid-cerebral artery PSV	28.0 (22.4-32.5)	27.6 (22.8-31.2)	0.956
Mid-cerebral artery PI	1.6 (1.4-1.8)	1.4 (1.2-1.7)	0.382
Ductus venosus PI	1.1 (1.0-1.4)	1.2 (0.9-1.3)	0.223

Abbreviations: S/D, systole/diastole; PI, pulsatility index; PSV, peak systolic velocity.
Data are presented as mean (±SD, range) or median (interquartile range). The Mann-Whitney test was used to compare the Doppler indexes between survived and non-survived fetuses.

Table 7. The Main Predictors for the Change in the CHOP Score After the Intervention

Variable	Beta	Standard Error	*P* Value
(Constant)	0.293	0.984	0.767
Age	-0.013	0.010	0.171
Gestational age at diagnosis	0.005	0.007	0.507
Fetal weight (recipient)	0.001	0.001	0.635
Fetal weight (donor)	0.001	0.001	0.797
Vertical pocket (recipient)	-0.035	0.022	0.113
Vertical pocket (donor)	-0.060	0.097	0.537
Quintero score	-0.156	0.079	0.042

Abbreviation: CHOP, Children's Hospital of Philadelphia.
Multivariable regression analysis was used to evaluate the relationship between the main predictors and the CHOP score.

TTTS have been expected due to abnormal circulating volumes as hypovolemia in the donors and adverse hypervolemia in recipients. Such cardiovascular changes can be manifested from the early stages of the disease and can even lead to lowering neonates' survival. According to the literature, the misbalancing twin-to-twin volumes can lead to both structural and functional abnormalities of fetuses such as ventricular hypertrophy, interventricular septal deviation, pulmonary hypertension, right to left shunt, mitral and tricuspid regurgitation, left and right ventricular outflow tract stenosis as well as cardiac malfunction-related brain injuries including hypoxic brain injury and intraventricular hemorrhage.[21] In addition, one recent review revealed the recipient twin had a higher risk of death due to absent/reversed flow in the umbilical artery before surgery. Also, in donors, there was only A/REDF in the umbilical artery, and the absence or reversal of waves in the ductus venous was associated with IUFD. There was no correlation observed between the occurrence of IUFD in donors and the preoperative myocardial performance index.[22]

Additionally, reduced diastolic ventricular filling in the recipient's twin along with increased arterial wall stiffness in donor twins can be observed in the progressive form of TTTS, leading to normal arterial wall stiffness as well as the diastolic functional state in both twins following the procedure.[21] It is obvious that the occurrence of vascular disorders such as changes in vascular resistance and blood flow velocity plays a major role in the occurrence of functional cardiac disorders in these patients. With the expansion of surgical methods, it is possible to improve the disease and, as a result, the possibility of correcting cardiovascular disorders, but the minor changes related to this improvement, as well as the factors that predict the improvement of cardiac and vascular function, have not yet been fully determined.

Based on the findings of the present study, first, a significant improvement was shown in the CHOP cardiovascular score and Doppler indices of both donor and recipient fetuses following SLPCV in TTTS patients. In line with such changes, the decrease in the CHOP score as a reliable score to determine the severity of cardiovascular manifestations was also revealed following the procedure. However, despite the improvement process in Doppler indices and CHOP score parameters, we still saw significant mortality in treated patients, so in both donor and recipient cases, we saw a significant decrease in patient fetuses' survival. Therefore, it seems that significant mortality of fetuses should not be searched only for cardiovascular disorders in these patients. One of the most important cases of death in these patients is preterm birth and its complications that remain a problem in patients after SLPCV. Neurodevelopmental impairment also affects the donor and recipient twins, which can lead to long-term morbidity.[23] Based on a previous study, the results indicated that after undergoing SLPCV, the overall survival rate was anticipated to range from 50% to 70%. Moreover, there was a 30% to 50% possibility of perinatal death, encompassing the entire population studied. Additionally, there was a 5% to 20% likelihood of long-term neurological impairment, even in cases where the cardiovascular bed appeared to be normal.[24]

Therefore, it seems that significant mortality of patients should not be searched only in cardiovascular and Doppler disorders in these patients. As in the model examined in the present study, limited Doppler indices were able to predict the intrauterine mortality of such patients. Nevertheless, a very important point that we found in the present study was that the occurrence of Doppler abnormalities in one fetus may be a prognostic factor in the survival of another fetus. Increased mid-cerebral artery PSV in the donor and higher Ductus Venous PI in the recipient could effectively predict intrauterine death in donor patients with TTTS undergoing SLPCV.

Also, the main determinants of intrauterine death in the recipients were increased umbilical artery PI and MCA PSV in donors. In other words, the occurrence of Doppler abnormalities in one fetus will decrease survival in itself and in another baby, which emphasizes the issue of careful evaluation and monitoring of Doppler abnormalities in one fetus in cases of involvement in the opposite fetus.

Other surveys revealed high MCA PSV and umbilical artery PI increased the risk of IUFD in recipients, and the cause of donor IUFD was absent or reverse a-wave ductus venosus.[22,25] Some studies identified a set of pre-laser Doppler parameters, including abnormal PI in the umbilical artery, ductus venosus, and MCA of the donor twin, which predict fetal death after the laser.[16] However, we do not have a united reference that has reached a consensus. More research is needed to reach that.

Regarding the positive relation between the CHOP score and Quintero classification, our results are similar to other studies.[15,26] Most literature, just like our study, found no correlation between the CHOP score and IUFD or fetuses' survival,[15,25] but Gapp-Born et al reported higher recipients' fetal loss in CHOP score ≥ 3.[25] This may be because the SLPCV coagulates the responsible anastomoses of imbalance hemodynamics and its cardiovascular impact. The effects of laser coagulation are likely to be enhanced over time as operators' skills and techniques improve, resulting in higher survival rates over time.

According to our study, the severity of TTTS was the most important factor in predicting the severity of CHOP cardiovascular score changes in such patients. TTTS causes an uneven distribution of blood volume, affecting the preload in the venous compartment. This imbalance leads to a notable increase in the umbilical venous flow in recipients compared to donors.[14] In advanced stages of the disease, as it becomes more severe, the umbilical venous flow diminishes in recipients, serving as an indication that the cardiac system is incapable of adequately accommodating the return of venous blood.[27] Thus, the severity of TTTS can be accompanied by more severe umbilical blood flow abnormality, thereby increasing the cardiac load of the disease.

This study, conducted in Iran, provides the initial findings and evaluation of the CHOP cardiovascular score, Doppler measurements, and survival outcomes in infants with a history of TTTS who underwent FLP. Notably, the strength of the study lies in its long-term follow-up, which enhances the robustness of the results. The study is currently in progress, and additional infants are being included for further observation. However, a significant limitation of the current study is that it does not account for prematurity and birthweight, which are recognized as crucial factors that can impact survival outcomes.

Conclusion

It can be finally concluded that a significant number of patients with TTTS suffer from cardiovascular disorders in the form of arterial blood flow abnormality, arterial wall stiffness, ventricular disturbances (ventricular hypertrophy), and diastolic heart failure, which manifests itself in the form of an increase in the CHOP score. In this regard, the SLPCV procedure can positively lead to the improvement of cardiovascular and Doppler parameters in these patients. It is interesting to note that the occurrence of Doppler disorders in one twin can lead to the occurrence of related disorders and IUFD in another twin, which indicates a strong correlation between the cardiovascular systems of two fetuses of twin pregnancies. In TTTS, the severity of the disease can be a powerful indicator of the severity of cardiovascular abnormalities.

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Competing Interests

None declared.

Ethical Approval

The study was conducted in compliance with ethical considerations for research involving human subjects and was reviewed and approved by the board at Tehran University of Medical Sciences. The research was conducted following the code of ethics with the identifier IR.TUMS.SHARIATI.REC.1401.008. Prior to participating, all subjects provided informed consent.

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