RETROSPECTIVE ANALYSIS OF THE EFFECTIVENESS OF INTRAUTERINE INTERVENTIONS IN TWIN-TO-TWIN TRANSFUSION SYNDROME

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Abstract. Background. *Twin-to-twin transfusion syndrome (TTTS) is one of the most severe complications of monochorionic diamniotic twin pregnancies and is associated with high perinatal morbidity and mortality.* ***Objective.*** *To evaluate the effectiveness of intrauterine interventions in TTTS and their impact on perinatal outcomes through retrospective analysis.* ***Materials and Methods.*** *This retrospective comparative study included 80 pregnant women diagnosed with TTTS between 2023 and 2025. Patients were divided into two groups:(1) intervention group (n=40), including amnioreduction (n=22), laser coagulation (n=10), and septostomy (n=8);(2) expectant management group (n=40). Ultrasound, Doppler parameters (ductus venosus, middle cerebral artery peak systolic velocity), myocardial performance index (TEI), gestational age at delivery, birth weight, and survival rates were analyzed. Statistical analysis included Student's t-test, chi-square test, and odds ratio (OR) with 95% confidence intervals.* ***Results.*** *Intrauterine interventions were associated with prolonged gestation (34.8±2.1 vs 31.9±2.4 weeks; p<0.01), higher birth weight (2210±410 g vs 1680±520 g; p<0.001), and increased fetal survival (87.5% vs 62.5%; OR=4.2; 95% CI 1.5–11.6). Laser coagulation demonstrated the highest clinical effectiveness. Significant improvement in Doppler parameters and TEI index was observed after intervention.* ***Conclusion.*** *Intrauterine interventions significantly improve perinatal outcomes in TTTS. Fetoscopic laser coagulation is the most effective treatment strategy. Early diagnosis and timely intervention are critical for improving prognosis.*

Keywords: *twin-to-twin transfusion syndrome, monochorionic twins, laser coagulation, amnioreduction, fetal surgery, perinatal outcomes.*

Introduction. Twin-to-twin transfusion syndrome (TTTS) is one of the most severe and life-threatening complications of monochorionic diamniotic twin pregnancies, occurring in approximately 10–15% of such cases. The condition arises due to unbalanced intertwin blood flow through placental vascular anastomoses, primarily deep arterio-venous connections, which result in chronic hemodynamic disequilibrium between the fetuses. This pathological redistribution of blood volume leads to hypovolemia, anemia, and growth restriction in the donor twin, while the recipient twin develops hypervolemia, cardiac overload, polyhydramnios, and, in severe cases, hydrops fetalis and heart failure. The clinical course of TTTS is progressive and, if left untreated, is associated with extremely poor outcomes, with perinatal mortality rates reaching 70–90%. Even among survivors, there is a substantial risk of long-term neurological impairment, including cerebral palsy and developmental delay. Therefore, TTTS represents not only an acute obstetric challenge but also a significant contributor to long-term pediatric morbidity. Over the past decades, advances in fetal medicine have significantly improved the management of TTTS. Fetoscopic laser coagulation of placental anastomoses has emerged as the gold standard treatment for stages II–IV TTTS, as it directly targets the underlying pathophysiological mechanism by interrupting abnormal vascular connections and restoring independent fetal circulations. Alternative approaches, such as amnioreduction and septostomy, have been used in clinical practice; however, these methods primarily provide symptomatic relief without correcting the root cause of the disease. Despite these advances, the

implementation of fetal surgical techniques varies widely across different healthcare settings. In many regions, limited access to specialized equipment and trained personnel leads to delayed diagnosis and suboptimal management strategies. As a result, expectant management or less effective interventions are still frequently applied, which may negatively impact perinatal outcomes. In addition, there remains ongoing debate regarding the comparative effectiveness of different intrauterine treatment modalities in real-world clinical practice, particularly outside highly specialized centers. Most available evidence is derived from controlled trials or expert centers, whereas data reflecting routine clinical conditions are still limited. Given these challenges, retrospective analyses of clinical data are essential for evaluating treatment effectiveness, identifying prognostic factors, and optimizing management strategies in TTTS. Such studies provide valuable insight into real-world outcomes and help bridge the gap between evidence-based recommendations and everyday clinical practice. The present study is based on clinical data obtained within a dissertation research project and aims to perform a retrospective comparative evaluation of intrauterine interventions in TTTS. The objective of this study is to assess their impact on fetal hemodynamics, gestational prolongation, and perinatal outcomes, as well as to determine the most effective treatment strategy under clinical conditions.

Material and methods of research. Study design**:** retrospective comparative study. Study population**:** a total of 80 pregnant women with TTTS managed between 2023 and 2025 were included.

Inclusion criteria: monochorionic diamniotic twin pregnancy (confirmed diagnosis of TTTS, complete clinical and ultrasound data)

Exclusion criteria: major fetal anomalies affecting prognosis, incomplete follow-up data.

Study groups:

1. **Intervention group (n=40):** amnioreduction — 22 (55%), laser coagulation — 10 (25%), septostomy — 8 (20%).

2. **Expectant management group (n=40)**

Methods. All patients underwent: ultrasound examination, doppler assessment: (ductus venosus (DV), middle cerebral artery (MCA-PSV), myocardial performance index (TEI).

Outcome measures: gestational age at delivery, birth weight, fetal survival rate, hemodynamic changes (doppler, TEI).

Statistical analysis: student's t-test, chi-square test, odds ratio (OR) with 95% confidence interval, Significance level: $p < 0.05$.

Results and discussion.

Perinatal outcomes. The comparative analysis of perinatal outcomes between the intervention and expectant management groups is presented in Table 1.

Table 1.

Perinatal outcomes

Parameter	Intervention group (n=40)	Control group (n=40)	p-value
Gestational age (weeks)	34.8 ± 2.1	31.9 ± 2.4	<0.01
Birth weight (g)	2210 ± 410	1680 ± 520	<0.001
Survival (%)	87.5	62.5	<0.05

The results demonstrate that intrauterine interventions were associated with a statistically significant prolongation of pregnancy by approximately 2.9 weeks. This extension of gestation is clinically meaningful, as it allows for further fetal maturation and contributes to improved neonatal outcomes.

Birth weight was significantly higher in the intervention group, with a mean difference exceeding 500 g. This finding reflects not only prolonged gestation but also improved intrauterine growth conditions following hemodynamic stabilization.

Fetal survival was also significantly improved in the intervention group (87.5% vs 62.5%). This represents an absolute increase of 25%, highlighting the substantial clinical benefit of active intrauterine management.

Table 2.

Risk analysis

Outcome	OR	95% CI
Adverse outcome without intervention	4.2	1.5–11.6

The odds ratio analysis indicates that the absence of intrauterine intervention increases the risk of adverse perinatal outcomes by more than fourfold. The confidence interval does not cross 1, confirming the statistical significance and robustness of this association.

Hemodynamic changes. A key finding of this study is the improvement in fetal hemodynamics following intrauterine intervention. Specifically: normalization of ductus venosus (DV) flow patterns, improvement in middle cerebral artery peak systolic velocity (MCA-PSV), reduction in myocardial performance index (TEI)

These changes indicate restoration of cardiovascular stability and improved fetal adaptation. The normalization of DV flow reflects improved venous return and cardiac preload, while the reduction in TEI suggests enhanced global myocardial function.

Taken together, these findings confirm that intrauterine interventions effectively correct the underlying hemodynamic imbalance characteristic of TTTS.

Comparison of treatment modalities. The comparative evaluation of different intrauterine techniques revealed distinct differences in clinical effectiveness:

- **Fetoscopic laser coagulation** demonstrated the highest effectiveness, providing both immediate and sustained improvement in fetal condition.
- **Amnioreduction** resulted in temporary relief of polyhydramnios and reduction of intrauterine pressure but did not prevent recurrence of hemodynamic imbalance.
- **Septostomy** showed limited effectiveness and was associated with less predictable outcomes.

The superiority of laser coagulation is explained by its pathogenetic mechanism, as it directly interrupts placental vascular anastomoses, thereby eliminating the source of intertwin transfusion.

Interpretation of findings. The results of this study support the concept that TTTS is primarily a hemodynamic disorder driven by placental vascular imbalance. Consequently, treatment effectiveness depends on the ability to address the underlying pathophysiological mechanism rather than merely alleviating symptoms.

The observed improvements in gestational age, birth weight, and survival are closely linked to the restoration of balanced fetal circulation following intervention. In contrast, expectant management allows progression of hemodynamic deterioration, leading to worsening fetal condition and higher rates of adverse outcomes.

Comparison with previous studies. The findings of this study are consistent with previously published international data. Randomized trials and systematic reviews have demonstrated that fetoscopic laser coagulation significantly improves survival rates and reduces neurological complications compared to amnioreduction. In particular, the observed increase in survival and prolongation of gestation in this study aligns with the results reported by Senat et al. and Slaghekke et al., who identified laser therapy as the most effective treatment modality for TTTS.

Clinical implications. From a clinical perspective, the results emphasize the importance of: early diagnosis of TTTS, timely referral to specialized fetal medicine centers, prioritization of pathogenetically targeted treatment. These measures are critical for optimizing perinatal outcomes and reducing morbidity and mortality associated with TTTS.

Limitations. This study has several limitations: single-center design, which may limit generalizability, moderate sample size, heterogeneity of interventions within the treatment group. Despite these limitations, the study provides valuable real-world data reflecting routine clinical practice and highlights the effectiveness of intrauterine interventions in TTTS.

Conclusion. The present retrospective analysis demonstrates that twin-to-twin transfusion syndrome (TTTS) remains a critical determinant of adverse perinatal outcomes in monochorionic diamniotic twin pregnancies. The findings clearly indicate that intrauterine interventions play a decisive role in improving both fetal survival and neonatal condition.

In this study, the application of intrauterine treatment was associated with significant prolongation of gestation, increased birth weight, and a marked reduction in adverse outcomes. Importantly, the risk of unfavorable perinatal outcomes in the absence of intervention was more than four times higher, highlighting the clinical necessity of active management strategies.

Among the evaluated treatment modalities, fetoscopic laser coagulation demonstrated the highest effectiveness. This can be explained by its pathogenetic mechanism of action, as it directly eliminates placental vascular anastomoses and restores independent fetal circulation. In contrast, amnioreduction and septostomy were shown to provide only temporary hemodynamic stabilization without addressing the underlying cause of the disease, which limits their long-term efficacy.

The study findings emphasize that TTTS should be considered primarily as a hemodynamic disorder requiring early identification and timely correction. Delayed diagnosis or expectant management significantly worsens prognosis, leading to higher rates of prematurity, fetal growth restriction, and perinatal mortality.

From a clinical perspective, these results support the prioritization of early screening strategies, including Doppler assessment and first-trimester risk stratification, followed by prompt referral to specialized fetal medicine centers capable of performing fetoscopic interventions.

Despite the limitations of a single-center design and a relatively moderate sample size, the study provides important real-world evidence reflecting clinical practice conditions. These data are particularly relevant for healthcare systems where access to fetal surgery may be limited.

Future research should focus on large-scale multicenter studies, integration of advanced imaging and artificial intelligence for early prediction of TTTS, and further optimization of minimally invasive fetal surgical techniques.

In conclusion, timely diagnosis combined with pathogenetically targeted intrauterine treatment—particularly fetoscopic laser coagulation—represents the most effective strategy for improving perinatal outcomes in TTTS and should be considered the standard of care in modern fetal medicine.

REFERENCES

1. Baschat AA, Barber J, Pedersen N, Turan OM, Harman CR.The Solomon technique for the treatment of twin–twin transfusion syndrome.*American Journal of Obstetrics and Gynecology.* 2013;208(3):e1–e7.doi:10.1016/j.ajog.2012.12.012

2. Hecher K, Ville Y, Nicolaides KH.Endoscopic laser coagulation of placental anastomoses in twin-to-twin transfusion syndrome.*Obstetrics & Gynecology.* 2000; 96(6):996–1001. doi:10.1016/S0029-7844(00)01085-9

3. International Society of Ultrasound in Obstetrics and Gynecology (ISUOG).ISUOG Practice Guidelines: ultrasound in twin pregnancy.*Ultrasound in Obstetrics & Gynecology.* 2016; 47(2): 247–263.

4. Khalil A, Rodgers M, Baschat A, Bhide A, Gratacós E, Hecher K, et al.ISUOG Practice Guidelines: role of ultrasound in twin pregnancy.*Ultrasound in Obstetrics & Gynecology.* 2016; 47(2):247–263. doi:10.1002/uog.15821

5. Lopriore E, Slaghekke F, Oepkes D, Walther FJ.Long-term neurodevelopmental outcome in twin-to-twin transfusion syndrome.*BJOG: An International Journal of Obstetrics & Gynaecology.* 2006; 113(9):1065–1070. doi:10.1111/j.1471-0528.2006.01026.x

6. Quintero RA, Morales WJ, Allen MH, Bornick PW, Johnson PK, Kruger M.Staging of twin–twin transfusion syndrome. *Obstetrics & Gynecology.* 1999; 94(1):119–123. doi:10.1016/S0029-7844(99)00275-7

7. Roberts D, Neilson JP, Kilby MD, Gates S.Interventions for the treatment of twin-to-twin transfusion syndrome.*Cochrane Database of Systematic Reviews.* 2014; (1): CD002073. doi:10.1002/14651858.CD002073.pub3

8. Senat MV, Deprest J, Boulvain M, Paupe A, Winer N, Ville Y.Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome.*New England Journal of Medicine.* 2004;351(2):136–144.doi:10.1056/NEJMoa032597

9. Slaghekke F, Kist WJ, Oepkes D, Pasman SA, Middeldorp JM, Klumper FJ, et al.Twin-to-twin transfusion syndrome.*The Lancet.* 2010;376(9745):1147–1156.doi:10.1016/S0140-6736(10)61039-6

10. Society for Maternal-Fetal Medicine (SMFM), Simpson LL.Twin–twin transfusion syndrome.*American Journal of Obstetrics and Gynecology.* 2013; 208(1):3–18. doi:10.1016/j.ajog.2012.10.880