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Neurodevelopmental outcome in Monochorionic Pregnancies complicated with TTTS following in utero laser treatment. A Systematic Review of the Literature and Meta – analysis.

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We use this protocol and it's working

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Keywords: Twin-to-Twin Transfusion syndrome, TTTS, Neurodevelopment, Fetoscopic Laser Surgery, FLS, term neurodevelopment outcome after fl, neurodevelopmental outcome, fetoscopic laser surgery, twin, utero laser treatment, term neurodevelopment outcome, transfusion syndrome, monochorionic pregnancy, children with quintero stage iv, amnioreduction

Abstract

TTTS also known as the Twin-To-Twin transfusion syndrome is a rare complication that only affects monochorionic pregnancies. Through the course of time and advancement of medicine, various therapeutic approaches have been utilized to treat the Twin-to-Twin transfusion syndrome. The two most common approaches offered to patients up to this day are the fetoscopic laser surgery (FLS) and the amnioreduction (AR). To properly evaluate the result of the applied treatment, the long-term neurodevelopment outcome after FLS should be taken into consideration. The authors will perform a review of the existing literature of the last 20 years on the neurodevelopmental outcome of twin-to-twin transfusion syndrome treated with fetoscopic laser surgery. Articles will be reviewed after searching through the biggest electronic medical libraries and the snowball procedure. Two authors will perform duplication removal, abstract screening and full-text article assessment. Communication, gross motor, fine motor, problem solving and personal / social skills will be assessed in children with Quintero stage IV during pregnancy.

Guidelines

Exclusion criteria

Alternative language publications, letters, older studies and omission of at least one inclusion criterion for the result set will classify a study as irrelevant and the authors will exclude them. All cell culture studies, case reports, animal studies, case series will be deemed irrelevant by the authors. For any studies with overlapping populations, the authors concluded that only one should be included, the most recent one.

Experimental workflow

The authors will identify the studies after querying 4 different electronic medical databases. Duplicates between the 4 result-sets will be removed. The titles of these papers will be reviewed and irrelevant articles will be excluded from the result-set. Two authors will screen the abstracts of the remaining articles to identify only studies that will be of interest to the subject of the review. After the unrelated will be excluded, the remaining articles will be then assessed for eligibility by reading their full content. The authors also will perform the snowball procedure to identify any potential studies of interest.

Data Extraction

Data extracted will include study characteristics, patient demographics, Quintero stage, treatment details, follow-up duration, and neurodevelopmental outcomes.

Data Synthesis and Meta-Analysis

Review Manager 5.4.1 will be used for meta-analysis. Odds ratios (OR) with 95% confidence intervals (CI) will be calculated. Heterogeneity will be assessed using the I^2 statistic. P-values 0.05 will be considered statistically significant. Forest plots will be generated to illustrate associations between Quintero stage IV and specific neurodevelopmental domains.

Materials

Materials and Methods

The authors will conduct a search through 4 of the biggest medical databases, MEDLINE, PUBMED, EMBASE and GOOGLE SCHOLAR. These databases will be utilized in order to search for relevant articles and studies up to November 2023 that describe outcomes for twin-to-twin transfusion syndrome pregnancies that were treated with fetoscopic laser surgery (FLS).

In order to include studies for reviewing, the authors will ensure that all relevant studies were referring to data that indicated an appropriate diagnosis of Twin-to-Twin transfusion syndrome. The studies should also utilize standard criteria for treatment and the treatment should have been performed via fetoscopic laser surgery (FLS). The studies should have also included data for neurologic impairment and morbidity that were collected from these patients at birth and up to their 6th year of life.

Materials and Methods

- 1 The authors will conduct a search through 4 of the biggest medical databases, MEDLINE, PUBMED, EMBASE and GOOGLE SCHOLAR. These databases will be utilized in order to search for relevant articles and studies up to November 2023 that describe outcomes for twin-to-twin transfusion syndrome pregnancies that were treated with fetoscopic laser surgery (FLS). The authors decided to only include studies from the last 20 years since the advancement of technology would make older methodologies obsolete.
- 2 The following terms will be used for searching: "ttts syndrome", "twin-to-twin transfusion syndrome", "ttts", "neurodevelopment", "neurodevelopmental", "neurodevelopmental outcome", "ttts syndrome neurodevelopment", "neurodevelopmental result", "twin-to-twin syndrome laser treatment", "twin-to-twin syndrome laser therapy", "ttts laser treatment", "ttts laser therapy", "ttts neurodevelopment", "ttts neurodevelopmental outcome", "ttts laser surgery uterus", "twin-to-twin syndrome laser surgery uterus", "ttts fls", "ttts fetoscopic laser surgery" and the query used (((ttts OR (ttts syndrome) OR (twin-to-twin transfusion syndrome)) AND ((laser OR (laser therapy) OR (laser treatment) OR (laser treatment uterus) OR (laser therapy uterus) OR fls OR (fetoscopic laser surgery))) AND (outcome OR result)). There will be no other restrictions that were applied to the search query and papers only written in English will be included.
- 3 Two authors independently will assess the results initially by reading the abstracts. For the remaining relevant results, the two authors will perform a read of the remaining papers and by applying the inclusion and exclusion criteria that were decided in the beginning of the study they will narrow down the result sample to the relevant studies that will be of interest. For any disagreements amongst authors, the decision will be taken by a third reviewer in order to reach consensus on inclusion or exclusion of a paper. Following the snowball procedure, the authors manually will search the remaining papers for relevant articles in an attempt to find other related papers via citation mining.

Inclusion criteria

- 4 In order to include studies for reviewing, the authors will ensure that all relevant studies were referring to data that indicated an appropriate diagnosis of Twin-to-Twin transfusion syndrome. The studies should also utilize standard criteria for treatment and the treatment should have been performed via fetoscopic laser surgery (FLS). The studies should have also included data for neurologic impairment and morbidity that were collected from these patients at birth and up to their 6th year of life.

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Ethics and Dissemination

- 9 No ethical approval will be required as this study is based on published literature. Findings will be disseminated via publication in a peer-reviewed journal and presentation at relevant conferences.

Conflicts of Interest & Funding

- 10 The authors declare no conflicts of interest. Funding: None.

Protocol references

References

1. van, K.J.; Koopman, H.; Oepkes, D.; Walther, F.; Lopriore, E. Long-term neurodevelopmental outcome in monochorionic twins after fetal therapy. *Early Hum Dev* **2011**, 87(9), 601–606.
2. Maschke, C.; Diemert, A.; Hecher, K.; Bartmann, P. Long-term outcome after intrauterine laser treatment for twin-twin transfusion syndrome. *Prenat Diagn* **2011**, 31(7), 647–653.
3. Graeve, P.; Banek, C.; Stegmann-Woessner, G.; Maschke, C.; Hecher, K.; Bartmann, P. Neurodevelopmental outcome at 6 years of age after intrauterine laser therapy for twin-twin transfusion syndrome. *Acta Paediatr* **2012**, 101(12), 1200–1205.
4. Quintero, R.; Morales, W.; Allen, M.; Bornick, P.; Johnson, P.; Kruger, M. Staging of twin-twin transfusion syndrome. *J Perinatol* **1999**, 19(8 Pt 1), 550–555.
5. Chon, A.; Korst, L.; Llanes, A.; Miller, D.; Ouzounian, J.; Chmait, R. Midtrimester isolated polyhydramnios in monochorionic diamniotic multiple gestations. *Am J Obstet Gynecol* **2014**, 211(3), 303.e1–5.
6. Cincotta, R.; Gray, P.; Phythian, G.; Rogers, Y.; Chan, F. Long term outcome of twin-twin transfusion syndrome. *Arch Dis Child Fetal Neonatal Ed* **2000**, 83(3), F171–F176.
7. Habli, M.; Michelfelder, E.; Cnota, J.; Wall, D.; Polzin, W.; Lewis, D.; et al. Prevalence and progression of recipient-twin cardiomyopathy in early-stage twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* **2012**, 39(1), 63–68.
8. Senat, M.; Deprest, J.; Boulvain, M.; Paupe, A.; Winer, N.; Ville, Y. Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. *N Engl J Med* **2004**, 351(2), 136–144.
9. Fisk, N.; Duncombe, G.; Sullivan, M. The basic and clinical science of twin-twin transfusion syndrome. *Placenta* **2009**, 30(5), 379–390.
10. Hopkins Medicine. Fetal Interventions – Fetoscopic Laser Surgery. Available online: <https://www.hopkinsmedicine.org/gynecology-obstetrics/specialty-areas/fetal-therapy/fetal-interventions-procedures/fetoscopic-laser-surgery> (accessed on 20 May 2025).
11. Miller, J. Twin to twin transfusion syndrome. *Transl Pediatr* **2021**, 10(5), 1518–1529.
12. Molina, S.; Papanna, R.; Moise, K.J.; Johnson, A. Management of Stage I twin-to-twin transfusion syndrome: an international survey. *Ultrasound Obstet Gynecol* **2010**, 36(1), 42–47.
13. Gordon, Z.; Fattal-Valevski, A.; Elad, D.; Jaffa, A. Controlled amnioreduction for twin-to-twin transfusion syndrome. *Ther Adv Reprod Health* **2022**, 16, 26334941221080727.

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