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SYSTEMATIC REVIEW

Right ventricular outflow tract obstruction in twin-to-twin transfusion syndrome undergoing laser surgery: A systematic review and meta-analysis

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Abstract

Introduction: We aimed to investigate the incidence, prenatal factors and outcomes of twin-to-twin transfusion (TTTS) with right ventricular outflow tract obstruction (RVOTO).

Material and methods: A systematic search was conducted to identify relevant studies published until February 2023 in English using the databases PubMed, Scopus and Web of Science. Studies reporting on pregnancies with TTTS and RVOTO were included. The random-effect model pooled the mean differences or odds ratios (OR) and the corresponding 95% confidence intervals. Heterogeneity was assessed using the I^2 value.

Results: A total of 17 studies encompassing 4332 TTTS pregnancies, of which 225 cases had RVOTO, were included. Incidence of RVOTO at time of TTTS diagnosis was 6%. In all, 134/197 (68%) had functional pulmonary stenosis and 62/197 (32%) had functional pulmonary atresia. Of these, 27% resolved following laser and 55% persisted after birth. Of those persisting, 27% required cardiac valve procedures. Prenatal associations were TTTS stage III (53% vs 39% in no-RVOTO), stage IV TTTS (28% in RVOTO vs 12% in no-RVOTO) and ductus venosus reversed a-wave (60% in RVOTO vs 19% in no-RVOTO). Gestational age at laser and gestational age at delivery were comparable between groups. Survival outcomes were also comparable between groups, including fetal demise of 26%, neonatal death of 12% and 6-month survival of 82% in RVOTO group. Findings were similar when subgroup analysis was done for studies including head-to-head analysis.

Conclusions: RVOT occurs in about 6% of the recipient twins with TTTS, especially in stages III and IV and those with reversed ductus venosus a-wave. The findings from this systematic review support the need for a thorough cardiac assessment of

Abbreviations: DV, ductus venosus; FLP, fetoscopic laser photocoagulation; GA, gestational age; PA, pulmonary atresia; PS, pulmonary stenosis; RVOTO, right ventricular outflow tract obstruction; TTTS, twins with twin-to-twin transfusion syndrome.

pregnancies complicated by TTTS, both before and after laser, to maximize perinatal outcome, and the importance of early diagnosis of TTTS and timely management.

KEYWORDS
fetoscopy, laser, meta-analysis, pulmonary atresia, pulmonary stenosis, recipient, right ventricular outflow tract, systematic review, twin-to-twin transfusion

1 | INTRODUCTION

Right ventricular outflow tract obstruction (RVOTO) such as pulmonary stenosis (PS) and pulmonary atresia (PA) can develop in monochorionic recipient twins with twin-to-twin transfusion syndrome (TTTS), with a reported incidence of 6.7%–12.9%.[1,2]

The exact pathophysiology of RVOTO is still not fully understood. The unbalanced share in the placental vascular anastomoses resulting in TTTS cause compensatory mechanisms against hypovolemia that increase the secretion of vasoactive mediators in the donor, which are also transferred to the recipient,[3] leading to the recipient twin developing polyuric polyhydramnios, hypertension and cardiac dysfunction and the donor twin developing oliguric oligohydramnios.[4] Therefore, TTTS has important direct effects on the cardiovascular system of the recipient twin affecting preload, cardiac function and afterload.[3]

Management options of TTTS include fetoscopic laser photocoagulation (FLP), amnioreduction, septostomy, selective reduction and expectant management,[5] with FLP being the standard care of management leading to increase in survival.[6] FLP disrupts the adverse feto-fetal hemodynamic communications,[7] thereby blocking the flow of vasoactive mediators from the donor to the recipient twin. Even though RVOTO regression has been achieved following FLP in many cases in recipient twins, persistence can still be seen, requiring postnatal cardiac intervention procedures.[1]

Our review aimed to investigate the incidence of RVOTO at TTTS diagnosis, following FLP and postnatally. We also aimed to investigate prenatal associations and outcomes of TTTS pregnancies with RVOTO.

Key message

Incidence of right ventricular outflow tract obstruction among TTTS pregnancies is 6% (68% had functional pulmonary stenosis and 32% had pulmonary atresia). Significant prenatal associations were TTTS stage III–IV and ductus venosus a-wave reversal. Survival was comparable to those without outflow obstruction.

2 | MATERIAL AND METHODS

The present study was conducted based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline 2020.[8] The study protocol was registered with PROSPERO (Registration code: CRD42023411483).

2.1 | Search strategy

A systematic search was performed in three electronic databases including PubMed, Scopus and Web of Science by two authors (MJ and AI), independently, from inception until February 2023. The search strategy included a combination of relevant medical subject heading (MeSH) terms and relevant keywords for ("fetofetal transfusion") AND ("outcome" OR "sequelae" OR "morbidity"). Further details, regarding the systematic search of literature are available in Table S1.

2.2 | Eligibility criteria

We defined our eligibility criteria based on the PICO framework: (P) Population: pregnancies complicated by TTTS; (I) Intervention: FLP; (C) Comparison: RVOTO vs no-RVOTO; (O) Outcome: survival. The exclusion criteria were absence of TTTS, narrative review articles, systematic reviews and conference abstracts and series with <3 cases.

2.3 | Data extraction and outcome measures

Two authors (MJ and AI) performed the data extraction using a standardized sheet. Any disagreement regarding the inclusion, exclusion or data extraction was resolved through a discussion with a third party (HJM). The standardized sheet included the following columns: name of the first author, publication year, period of the study, country, institute, design of the study, study inclusion and exclusion, number of cases, gestational age (GA) at diagnosis, TTTS stage, Doppler studies including umbilical artery and ductus venosus (DV), ECHO findings including tricuspid regurgitation (TR), GA at delivery, and survival including fetal demise, neonatal death and 6-month survival. In the case of overlap or duplications in patients between studies, the study with the larger sample size was included for review. Overlap of the study populations was assessed by authors and institution where the study was performed and the year

of publication. The overlapped studies were not excluded if they reported on different variables.

The diagnosis of PS was based on high peak systolic velocity (>100 cm/s) and turbulent flow across the pulmonary valve, with or without thickened and domed pulmonary valve cusps, and with or without the presence of tricuspid regurgitation. PA was diagnosed in the absence of forward flow across the pulmonary valve during systolic and reverse flow in the ductus arteriosus.[9]

2.4 | Quality assessment

The Newcastle–Ottawa Scale (NOS) for cohort studies was used to evaluate the quality of included cohort or case–control studies and the risk of bias. A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability. A score above seven is considered to be high quality.[10]

2.5 | Statistical analysis and data synthesis

We calculated the pooled proportions and their 95% confidence intervals. Heterogeneity of the included studies was assessed graphically and statistically by Higgins I^2 test. The weight given to each study was decided according to the inverse variance method in order to minimize the imprecision of the pooled effect estimate. Aa subgroup analysis was then done to include studies reporting head-to-head comparison of RVOTO vs no-RVOTO and the Pooled effect sizes were presented using mean difference (MD) or odds ratio (OR), using the Mantel–Haenszel test, with 95% confidence interval (CI) for continuous and categorical variables, respectively. The random effect model was used. Variables that were reported in at least two studies were included in the analysis. To test the overall significance of the random model, the *z*-test was performed. Potential publication bias was graphically assessed by creating funnel plots for each of the groups with an exploratory aim. Tests for funnel plot asymmetry were not used when the total number of publications included for each outcome was less than 10. In this case, the power of the tests was too low to distinguish chance from real asymmetry. RSTUDIO[11] (RStudio, Inc.) was used for the statistical analysis and creating forest and funnel plots.

3 | RESULTS

3.1 | Search strategy and study characteristics

A total of 1361 articles were retrieved from three databases. Of those articles, 654 were excluded for duplication. The remaining 707 studies were screened for eligibility (Figure 1). Title and abstract screening resulted in 61 potentially eligible studies. After a full-text

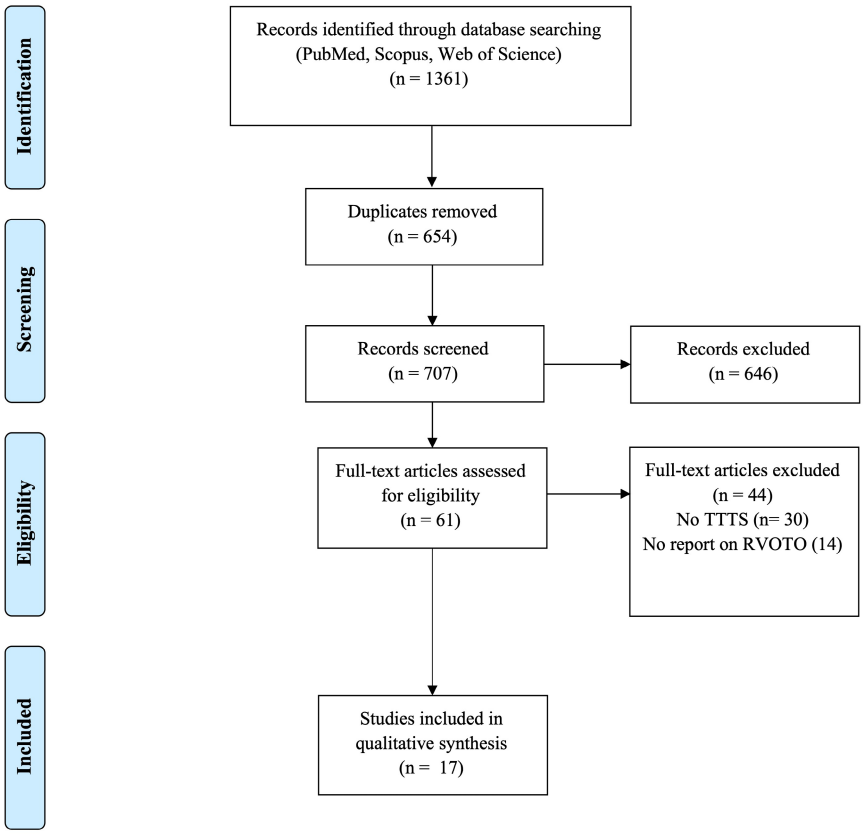

FIGURE 1 PRISMA flow chart of search and selection process.

TABLE 1 Characteristics of the 17 studies included in the systematic review.

First author	Year of publication	Study period	Country	Institute	Study design	Eligibility criteria	Total study population (*n*)	Recipients with RVOTO (*n*)	Donors with RVOTO (*n*)
Alrais[12]	2011	2000–2009	USA	Children's hospital, University of California, San Francisco	Retrospective cohort	TTTS at any stage	202	5	N/A
Eschbach[13]	2018	2015–2017	The Netherlands	The Leiden University Medical Center	Retrospective cohort	TTTS at any stage	124	16	N/A
Eschbach[14]	2016	2004–2015	The Netherlands	The Leiden University Medical Center	Retrospective cohort	TTTS at any stage	385	13	1
Espinoza[15]	2020	2012–2018	USA	Baylor College of Medicine	Retrospective cohort	TTTS at any stage	126	5	N/A
Gray[16]	2009	2002–2006	Australia	Mater Mother's Hospital, Brisbane	Retrospective cohort	TTTS at any stage	16	3	N/A
Herberg[17]	2005	–	Germany	Barmbek Hospital	Prospective cohort	TTTS at any stage	51	4	N/A
Lopriore[18]	2007	2002–2005	The Netherlands	The Leiden University Medical Center	Prospective cohort	TTTS at any stage, exclude non-cardiac congenital anomalies, triplets, and TTTS not treated by FLP	112	3	N/A
McPherson[19]	2019	–	USA	Marshfield Clinic Twin Cohort and Wisconsin Stillbirth Service Program	Retrospective cohort	TTTS at any stage	45	2	N/A
Michelfelder[20]	2014	2004–2010	USA	Cincinnati Children Hospital	Retrospective cohort	TTTS at any stage	610	53	N/A
Murata[21]	2019	2010–2015	Japan	Yamaguchi University Graduate school of Medicine	Retrospective cohort	TTTS at any stage, exclude TRAP, laser surgery after 26 weeks of gestation, recipient demise after laser therapy, and severe fetal congenital malformations	90	6	N/A
Oritz[22]	2016	–	Spain	Hospital in Barcelona	Prospective cohort	TTTS at any stage, exclude triplets or higher number	260	28	N/A
Pruetz[23]	2017	2006–2015	USA	Children's Hospital, Los Angeles	Prospective cohort	TTTS at any stage	259	28	N/A
Springer[24]	2014	2002–2012	Austria	Medical University of Vienna	Retrospective cohort	TTTS at any stage, excludes pregnancies that did not deliver at referred center	762	8	N/A
Van Mieghem[4]	2013	1998–2011	Canada	Mount Sinai Hospital	Retrospective cohort	TTTS at any stage	22	8	N/A

TABLE 1 (Continued)

First author	Year of publication	Study period	Country	Institute	Study design	Eligibility criteria	Total study population (*n*)	Recipients with RVOTO (*n*)	Donors with RVOTO (*n*)
Chang[1]	2022	2007–2021	Taiwan	Chang Gung Memorial Hospital	Retrospective cohort	TTTS at any stage, excludes cardiac and genetic abnormalities	187	14	N/A
Faiola[2]	2021	2009–2018	Italy	Fetal Therapy Unit of Vittore Buzzi Children Hospital	Retrospective cohort	TTTS at any stage, exclude pregnancies complicated by multiple structural abnormalities, chromosomal/genetic syndromes, TRAP sequence, monoamnionicity or without perinatal follow-up	891	14	N/A
Takano[7]	2022	2015–2021	Japan	Toho University Omori Medical Center	Prospective cohort	TTTS at any stage	190	14	N/A

assessment was performed, 17 studies encompassing 4332 TTTS pregnancies were included. Study characteristics are presented in Table 1. Included studies were published between 2005 and 2022. Twelve studies were retrospective and 5 were prospective cohorts. Most studies investigated the acquired RVOTO in recipient twins ($n = 224$ recipient twins with RVOTO). One study investigated RVOTO in both recipient and donor twins, of which there were 13 recipients and one donor with RVOTO out of 385 TTTS pregnancies.[14]

3.2 | Incidence of RVOTO

The incidence of RVOTO in TTTS was 6% (95% CI 4–10). Type of RVOTO was reported for 197 recipient twins, of which 134 (68%) had PS and 62 (32%) PA. Of these, 27% (95% CI 15–43) resolved following FLP for TTTS. A total of 55% (95% CI 36–73) of RVOTO cases persisted after birth. Among the cases of RVOTO that persisted, 27% (95% CI 16–42) required cardiac valve procedures (Figure S1).

3.3 | Prenatal associations and outcomes in TTTS pregnancies with RVOTO undergoing FLP

Stage III TTTS presented more frequently in RVOTO (53%, 95% CI 40–66) vs no-RVOTO (39%, 95% CI 36–43) than in those with stage IV TTTS (28%, 95% CI 16–44) in RVOTO vs no-RVOTO (12%, 95% CI 2–55). Few studies presented TTTS stage as combined III and IV and was noted to be more frequent in RVOTO (77%, 95% CI 42–48) vs no-ROVOT (45%, 95% CI 42–48) (Table 2, Figures S5–S9).

A DV reversed a-wave appeared more often in the RVOTO group (60%, 95% CI 51–69) than in the no-RVOTO Group (19%, 95% CI 16–22). Tricuspid regurgitation was also observed more frequently in RVOTO (66%, 95% CI 45–82) than in the no-RVOTO group (38%, 95% CI 9–79). GA at laser and GA at delivery were comparable between groups (Table 2, Figures S10–S13).

Survival outcomes were either comparable or not higher than the no-RVOTO group which included IUFD (26%, 95% CI 19–34) in RVOTO than in no-RVOTO (31%, 95% CI 10–64). The recipient demise was 25% (95% CI 18–33) in RVOTO vs 20% (95% CI 12–32) in no-RVOTO. Donor demise was 14% (95% CI 6–30) in RVOTO vs 26% (95% CI 14–43) in no-RVOTO. Neonatal death was 12% (95% CI 6–24) in RVOTO vs 11.6% (95% CI 7–15) in no-RVOTO. The 6-month survival was 82% (9% CI 51–95) in RVOTO vs 80.6% (95% CI 60–93) in no-RVOTO (Table 2, Figures S14–S18).

3.4 | Subgroup analysis for studies reporting head-to-head analysis

We performed subgroup analysis for the studies that reported head-to-head comparison for prenatal associations and outcomes between RVOTO and no-RVOTO pregnancies. Five studies reported such comparisons.[13,14,21,22] TTTS stage IV, a combination of stage III

TABLE 2 Pooled proportions of factors and outcomes in monochorionic twin pregnancies with twin-to-twin transfusion syndrome with or without right ventricular outflow tract obstruction.

	RVOTO			No-RVOTO		
Variable	Studies (*n*)	*N*	Pooled proportion % (95% CI)	Studies (*n*)	*N*	Pooled proportion % (95% CI)
GA at laser therapy (weeks)	13	224	19.9 (19–20)	7	1321	19.7 (18–21)
TTT stage I	4	50	17 (9–31)	3	365	18 (14–22)
TTT stage II	6	114	15 (5–37)	3	365	35 (30–40)
TTT stage III	4	722	53 (40–66)	6	117	39 (36–43)
TTT stage IV	7	120	28 (16–44)	5	735	12 (2–55)
TTT stage III–IV	7	145	77 (63–87)	5	954	45 (42–48)
DV reversed a-wave	7	124	60 (51–69)	4	720	19 (16–22)
TR	9	152	66 (45–82)	4	649	38 (9–79)
IUFD	9	153	26 (19–34)	4	403	31 (10–64)
Recipient fetal demise	6	130	25 (18–33)	2	281	20 (12–32)
Donor fetal demise	3	35	14 (6–30)	2	257	26 (14–43)
GA at delivery, weeks	11	224	33.1 (32–33)	11	1575	33.1 (32–33)
Neonatal death	4	61	12 (6–24)	4	203	11.6 (7–15)
6-month survival	4	51	82 (51–95)	4	201	80.6 (60–93)

Abbreviations: DV, ductus venosus; GA, gestational age; IUFD, intrauterine fetal demise; RVOTO, right ventricular outflow tract obstruction; TR, tricuspid regurgitation; TTTS, twin-to-twin transfusion syndrome.

and IV, and reversed DV a-wave were significantly more common in the RVOTO group (OR 3.1, 95% CI 1.5–6.2; OR 1.66, 95% CI 1.1–2.3; OR 2.85, 95% CI 1.6–4.8, respectively). There were no differences in TTTS stage I, II, GA at diagnosis, GA at delivery, single fetal demise or recipient demise between groups (Figures S19–S29).

3.5 | Risk of bias assessment

Small study effect was not evident for any outcome. Risk of bias assessed using NOS for cohort showed a minimum score of seven in the included studies (Table 3).

4 | DISCUSSION

Our meta-analysis demonstrates that the incidence of RVOTO in pregnancies complicated by TTTS undergoing FLP is 6%, of which 68% had functional PS and 32% had functional PA. Of these, 27% resolved after laser therapy and 55% persisted to birth. Of those that persisted following birth, 27% required cardiac valve procedures. Potential prenatal associations were TTTS stage III–IV and DV reversed a-wave. TTTS pregnancies with RVOTO did not have higher fetal demise for recipient or donor, neonatal death or a lower 6-month survival.

RVOTO affects almost exclusively the recipient twin as a consequence of hypertensive cardiomyopathy in TTTS, for a reason not yet fully understood.[14] Monochorionic twins complicated by TTTS experience a similar phenomenon, where the hypoperfusion of the donor twin leads to upregulation of renin secretion and activation of the renin–angiotensin–aldosterone system.[25] Renin mRNA is increased in donor kidneys and downregulated in recipient kidneys: however, equally elevated cord blood renin levels have been observed in both twins by the transfer through placental anastomoses of renin–angiotensin–aldosterone system. It has yet to be explained why RVOTO occurs almost exclusively in the recipient twin and not in the donor twin,[3] although one study reported one donor twin affected with RVOTO.[13]

FLP has become the predominant therapy for TTTS that has been shown to improve perinatal survival and neurologic outcomes. In spite of the success of laser surgery as a curative treatment for TTTS and the massive cardiovascular improvements seen in affected twins, the phenomenon of persistence or development of CHD remains unresolved.[26] RVOTO in TTTS is considered an acquired (functional) finding.

In our study, the incidence of RVOTO in recipient twins in pregnancies complicated by severe TTTS cases was 6% at time of TTTS diagnosis, a much higher incidence than prenatal congenital heart disease, which indicates that fetal echocardiography needs to be performed in pregnancies with TTTS to identify any cardiac anomalies and for those fetuses to undergo the proper follow-up as needed following laser and following birth. RVOTO mainly comprises PA and PS; in our review, the incidence of PS in recipient twins with RVOTO was 68% and the incidence of PA was 32%. Other studies have reported the risk of PA to be 45%,[20] 19.2%[26] and 42.8%, respectively.[22] PA has a poorer prognosis than PS,[27]

TABLE 3 Risk of bias assessment of the included studies using the Newcastle–Ottawa Scale.

Authors	Selection				Comparability	Outcome			Total
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest not presented at beginning of study		Assessment of outcome	Enough follow-up	Adequacy of follow-up	
Alrais 2011[12]	*		*	*	*	*	*	*	7
Eschbach 2018[13]	*	*	*	*	**	*	*	*	9
Eschbach 2016[14]	*	*	*	*	**	*	*	*	9
Espinoza 2020[15]	*		*	*	*	*	*	*	7
Gray 2009[16]	*	*	*	*	**	*	*	*	9
Herberg 2005[17]	*		*	*	*	*	*	*	7
Lopriore 2007[18]	*		*	*	*	*	*	*	7
McPherson 2014[19]	*		*	*	*	*	*	*	7
Michelfelder 2019[20]	*		*	*	*	*	*	*	7
Murata 2016[21]	*	*	*	*	**	*	*	*	9
Oritz 2016[22]	*	*	*	*	**	*	*	*	9
Pruetz 2017[23]	*	*	*	*	**	*	*	*	9
Springer 2014[24]	*	*	*	*	**	*	*	*	9
Van Mieghem 2013[4]	*		*	*	*	*	*	*	7
Chang 2022[1]	*	*	*	*	**	*	*	*	9
Faiola 2021[2]	*		*	*	*	*	*	*	7
Takano 2022[7]	*		*	*	*	*	*	*	7

which might explain the comparable survival outcomes between groups in our systematic review.

The onset of TTTS early in gestation was reported as a prenatal association for RVOTO in TTTS recipient twins with a mean of 17.3 weeks in RVOTO compared with a mean of 20.3 weeks in no-RVOTO;[14] however, in our systematic review, GA at time of diagnosis was not different between TTTS pregnancies with or without RVOT with mean of 19 weeks. Although one study showed that occurrence of RVOTO in TTTS does not differ among different TTTS stages,[13] other reports and our systematic review showed a higher prevalence of RVOTO in stages III–IV. Recipient twins in cases of stage IV TTTS are more likely to develop cardiomyopathy and cardiac hypertrophy. Tricuspid regurgitation and aortic flow reversal through the ductus arteriosus in TTTS can cause the pulmonary valve flow to decrease, which can lead to narrowing and stenosis of the fetal pulmonary valve in the recipient twin. This may explain why stage IV TTTS is a risk factor for RVOTO. However, because cardiomyopathy occurs less often in TTTS donor twins, RVOTO has been reported less often in donor twins.[1]

The strengths of this review are the thorough search and assessment of three large databases resulting in a large sample size of TTTS recipient fetuses with RVOTO.

The small number of cases in some of the included studies, their retrospective non-randomized design, heterogeneity in prenatal management, and different follow-up periods represent the major limitations. Some of the variables that we intended to collect and stratify were only reported by small number of studies, limiting our ability to include them in the analysis. The findings are also subject to potential publication bias because of the nature of some outcomes. In addition, the small number of studies limits the reliability of formal tests.

5 | CONCLUSION

Our meta-analysis provides vital information when counseling TTTS pregnancies regarding the incidence, potential prenatal associations and outcomes of RVOTO. Fetal echocardiography should be performed upon TTTS diagnosis and following laser therapy and birth as needed. PS was more common that PA and cases most commonly involved recipient fetuses. The presence of RVOTO at advanced TTTS stages and those with DV flow abnormalities emphasizes on the importance of early detection and timely management of TTTS. Survival outcomes including fetal demise, neonatal death and survival up to 6 months of life were comparable in pregnancies with and without RVOTO.

AUTHOR CONTRIBUTIONS

Hiba J. Mustafa: study design, methodology, and manuscript preparation. Muhammad Jawwad and Ayesha Iqbal Mansoor: article search, full-text review, and data extraction. Giorgio Pagani and Franscesco D'Antonio: statistical analysis. Asma Khalil: Expert review of methodology, analysis, results, and manuscript.

CONFLICT OF INTEREST STATEMENT

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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REFERENCES

1. Chang YL, Chao AS, Chang SD, Cheng PJ, Li WF, Hsu CC. Incidence, prognosis, and perinatal outcomes of and risk factors for severe twin-twin transfusion syndrome with right ventricular outflow tract obstruction in the recipient twin after fetoscopic laser photocoagulation. *BMC Pregnancy Childbirth*. 2022;22:326.
2. Faiola S, Casati D, Laoreti A, et al. Right ventricular outflow tract abnormalities in monochorionic twin pregnancies without twin-to-twin transfusion syndrome: prenatal course and postnatal long-term outcomes. *Prenat Diagn*. 2021;41:1510-1517.
3. Wohlmuth C, Boudreaux D, Moise KJ, et al. Cardiac pathophysiology in twin–twin transfusion syndrome: new insights into its evolution. *Ultrasound Obstet Gynecol*. 2018;51:341-348.
4. Van Mieghem T, Martin AM, Weber R, et al. Fetal cardiac function in recipient twins undergoing fetoscopic laser ablation of placental anastomoses for stage IV twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol*. 2013;42:64-69.
5. Di Mascio D, Khalil A, D'Amico A, et al. Outcome of twin-twin transfusion syndrome according to Quintero stage of disease: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2020;56:811-820.
6. Stirnemann J, Slaghekke F, Khalek N, et al. Intrauterine fetoscopic laser surgery versus expectant management in stage 1 twin-to-twin transfusion syndrome: an international randomized trial. *Am J Obstet Gynecol*. 2021;224:528.e1-528.e12.
7. Takano M, Hine K, Nagasaki S, et al. Different expressions of cardiac biomarkers between different types of acquired right ventricular outflow tract abnormality in monochorionic twins. *Prenat Diagn*. 2022;42:1448-1457.
8. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *PLoS Med*. 2021;18:e1003583.
9. Baumgartner H, Hung J, Bermejo J, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *Eur J Echocardiogr*. 2009;10:1-25.
10. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25:603-605.
11. RStudio: Integrated Development Environment for R. 2020.
12. Alrais F, Feldstein VA, Srivastava D, Gosnell K, Moon-Grady AJ. Monochorionic twins discordant for congenital heart disease: a referral center's experience and possible pathophysiologic mechanisms. *Prenat Diagn*. 2011;31:978-984.
13. Eschbach SJ, ten Harkel ADJ, Middeldorp JM, et al. Acquired right ventricular outflow tract obstruction in twin-to-twin transfusion syndrome; a prospective longitudinal study. *Prenat Diagn*. 2018;38:1013-1019.
14. Eschbach SJ, Boons L, Van Zwet E, et al. Right ventricular outflow tract obstruction in complicated monochorionic twin pregnancy. *Ultrasound Obstet Gynecol*. 2017;49:737-743.
15. Espinoza J, Furtun BY, Kailin JA, et al. Umbilical artery Doppler patterns and right ventricular outflow abnormalities inTwin-TwinTransfusion syndrome. *J Ultrasound Med*. 2021;40:71-78.

16. Gray PH, Ward C, Chan FY. Cardiac outcomes of hydrops as a result of twin-twin transfusion syndrome treated with laser surgery. *J Paediatr Child Health*. 2009;45:48-52.
17. Herberg U, Gross W, Bartmann P, Banek CS, Hecher K, Breuer J. Long term cardiac follow up of severe twin to twin transfusion syndrome after intrauterine laser coagulation. *Heart*. 2006;92:95-100.
18. Lopriore E, Sueters M, Middeldorp JM, Oepkes D, Vandenbussche FP, Walther FJ. Neonatal outcome in twin-to-twin transfusion syndrome treated with fetoscopic laser occlusion of vascular anastomoses. *J Pediatr*. 2005;147:597-602.
19. McPherson E, Korlesky C, Hebbring S. Cardiac anomalies in liveborn and stillborn monochorionic twins. *Clin Med Res*. 2020;18:58-67.
20. Michelfelder E, Gottliebson W, Border W, et al. Early manifestations and spectrum of recipient twin cardiomyopathy in twin-twin transfusion syndrome: relation to Quintero stage. *Ultrasound Obstet Gynecol*. 2007;30:965-971.
21. Murata S, Nakata M, Sugino N. Prevalence of right ventricular outflow tract abnormalities among recipients in twin-twin transfusion syndrome after fetoscopic laser surgery in 90 consecutive cases. *J Med Ultrason*. 2001;2020(47):117-121.
22. Ortiz JU, Masoller N, Gomez O, et al. Rate and outcomes of pulmonary stenosis and functional pulmonary atresia in recipient twins with twin-twin transfusion syndrome. *Fetal Diagn Ther*. 2017;41:191-196.
23. Pruetz JD, Votava-Smith JK, Chmait HR, Korst LM, Llanes A, Chmait RH. Recipient twin circular shunt physiology before fetal laser surgery. *J Ultrasound Med*. 2017;36:1595-1605.
24. Springer S, Mlczoch E, Krampl-Bettelheim E, et al. Congenital heart disease in monochorionic twins with and without twin-to-twin transfusion syndrome. *Prenat Diagn*. 2014;34:994-999.
25. Paul M, Poyan Mehr A, Kreutz R. Physiology of local renin-angiotensin systems. *Physiol Rev*. 2006;86:747-803.
26. Pruetz JD, Sklansky M, Detterich J, Korst LM, Llanes A, Chmait RH. Twin-twin transfusion syndrome treated with laser surgery: postnatal prevalence of congenital heart disease in surviving recipients and donors. *Prenat Diagn*. 2011;31:973-977.
27. Daubeney PE, Sharland GK, Cook AC, Keeton BR, Anderson RH, Webber SA. Pulmonary atresia with intact ventricular septum: impact of fetal echocardiography on incidence at birth and postnatal outcome. UK and Eire collaborative study of pulmonary atresia with intact ventricular septum. *Circulation*. 1998;98:562-566.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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