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Facultad de Medicina, Universidad de Chile

Cardiopatías en Síndrome de Transfusión Feto-fetal (STFF)

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Introducción

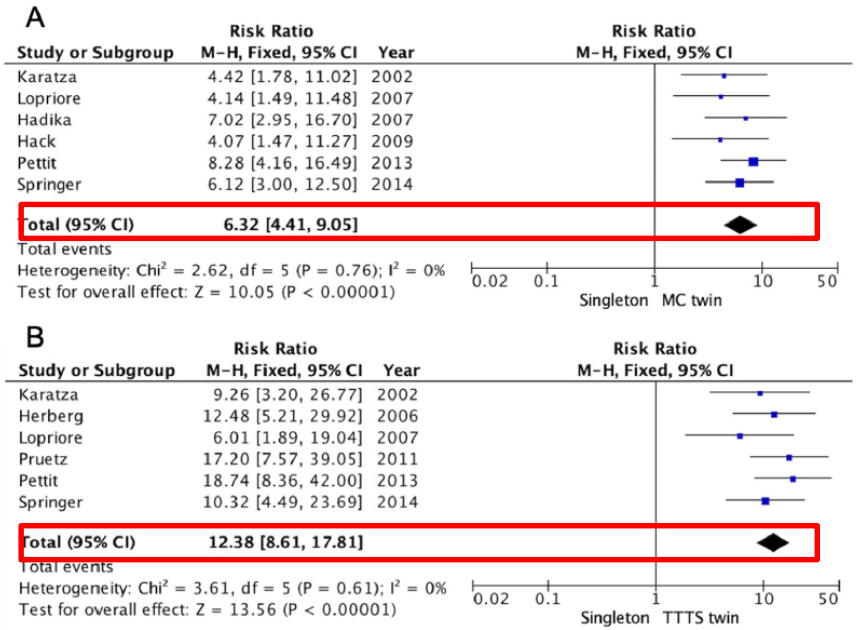
- El síndrome de transfusión feto-fetal (STFF) se caracteriza por un desbalance hemodinámico provocado por anastomosis vasculares placentarias.

- **Feto donante:** Hipovolemia, oliguria, oligohidroamnios.
- **Feto receptor:** Hipervolemia, poliuria, polihidroamnios.

- Ocurre en alrededor de 10-15% de los embarazos monocoriales.

- Los embarazos monocoriales tienen un riesgo aumentado de cardiopatías congénitas en comparación con embarazos bicoriales y embarazos únicos. Este riesgo es mayor en presencia de STFF.

Introducción



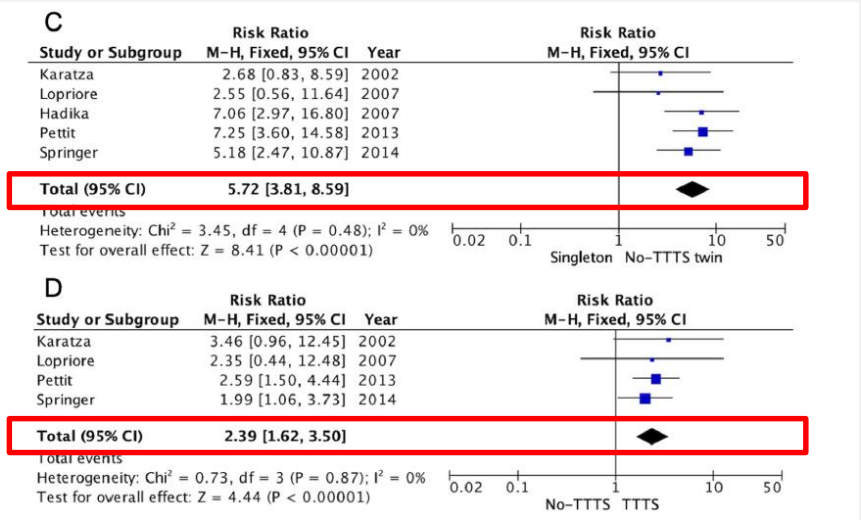


Figure 2. Risk of CHDs in MC twins with and without TTTS. (**A**) MC twins vs. singletons, (**B**) MC twins with TTTS vs. singletons, (**C**) MC twins without TTTS vs. singletons, (**D**) MC twins with TTTS vs. MC twins without TTTS. Risk ratios with 95% confidence intervals (CIs) were calculated by a fixed effect model. The pooled risk ratio is represented by a black diamond, where diamond width corresponds to 95% CI bounds.

Gijtenbeek M, Shirzada MR, Ten Harkel ADJ, Oepkes D, C Haak M. Congenital Heart Defects in Monochorionic Twins: A Systematic Review and Meta-Analysis. J Clin Med. 2019 Jun 24;8(6):902.

Epidemiología

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Prevalencia de cardiopatías congénitas en embarazos monocoriales

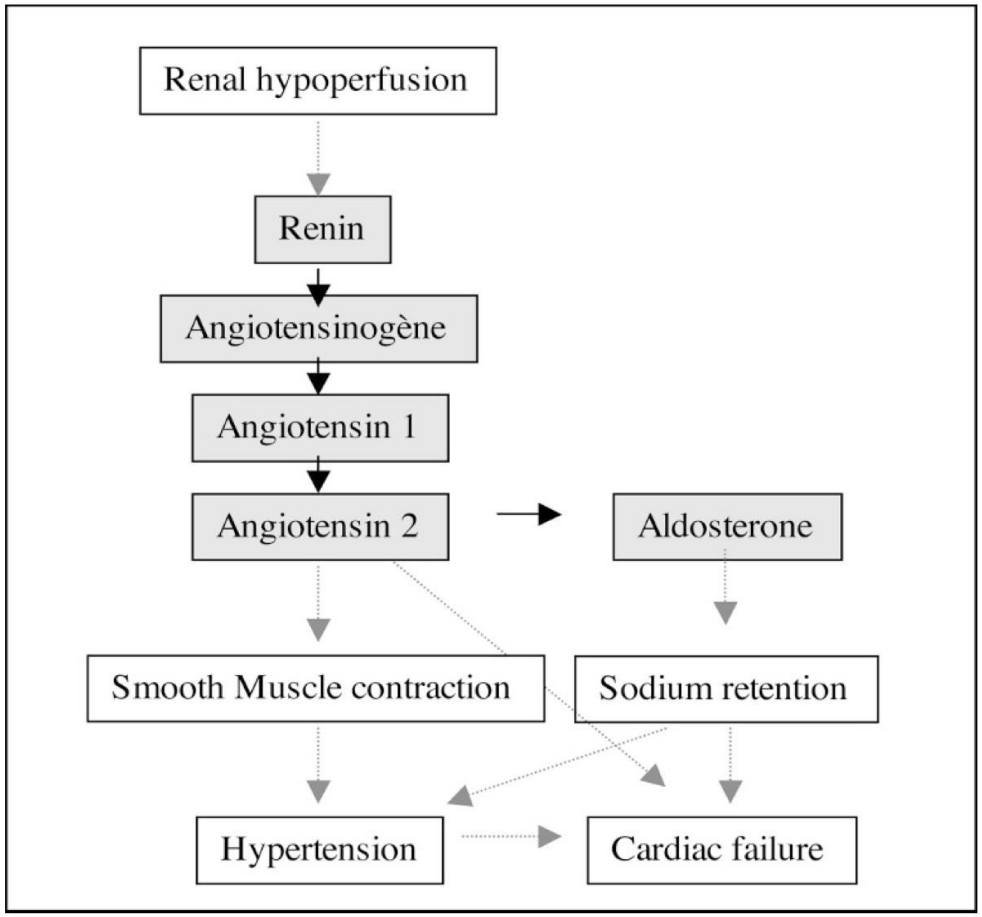
- VSD 25.9/1000
- RVOTO 22.3/1000
- ASD 13.6/1000
- CoA 2.1/1000
- AS 2.6/1000

- *TOF 0.9/1000*
- *TGA 0.9/1000*

En STFF existe un **RR de 70 (95% IC: 27-179, p<0.001) para RVOTO** (35/1000 vs 0.5/1000 en embarazos únicos)

Gijtenbeek M, Shirzada MR, Ten Harkel ADJ, Oepkes D, C Haak M. Congenital Heart Defects in Monochorionic Twins: A Systematic Review and Meta-Analysis. J Clin Med. 2019 Jun 24;8(6):902.

Fisiopatología



Mahieu-Caputo D, Meulemans A, Martinovic J, Gubler MC, Delezoide AL, Muller F, Madelenat P, Fisk NM, Dommergues M. Paradoxic activation of the renin-angiotensin system in twin-twin transfusion syndrome: an explanation for cardiovascular disturbances in the recipient. Pediatr Res. 2005 Oct;58(4):685-8.

Fisiopatología

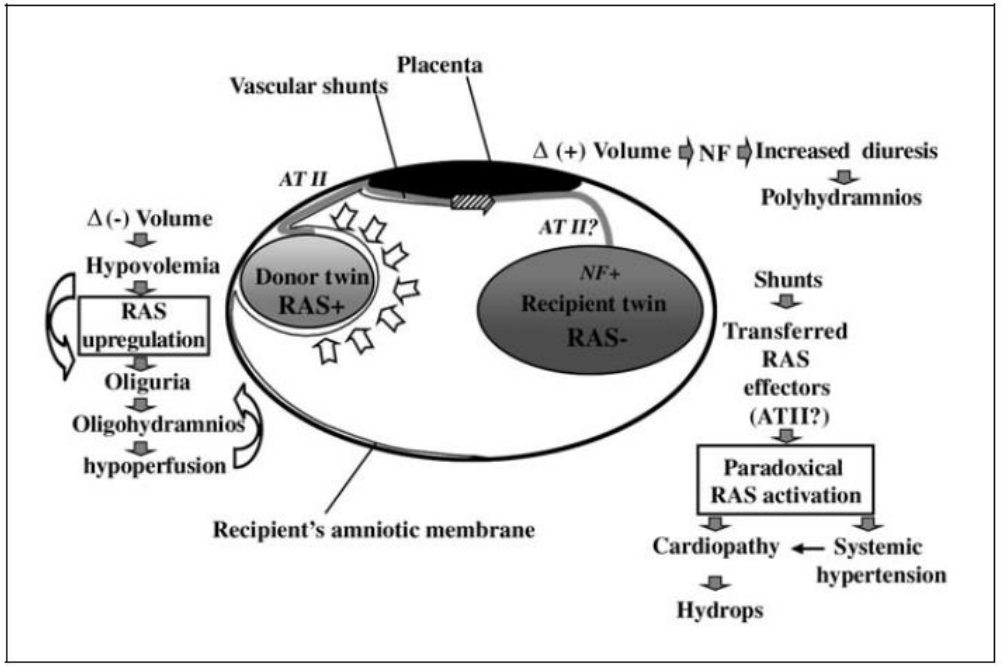


Fig. 1. Pathogenesis of severe TTTS: involvement of the RAS. ATII = Angiotensin II; NF = natriuretic factor.

Mahieu-Caputo D, Muller F, Joly D, Gubler MC, Lebidois J, Fermont L, Dumez Y, Dommergues M. Pathogenesis of twin-twin transfusion syndrome: the renin-angiotensin system hypothesis. Fetal Diagn Ther. 2001 Jul-Aug;16(4):241-4.

Fisiopatología

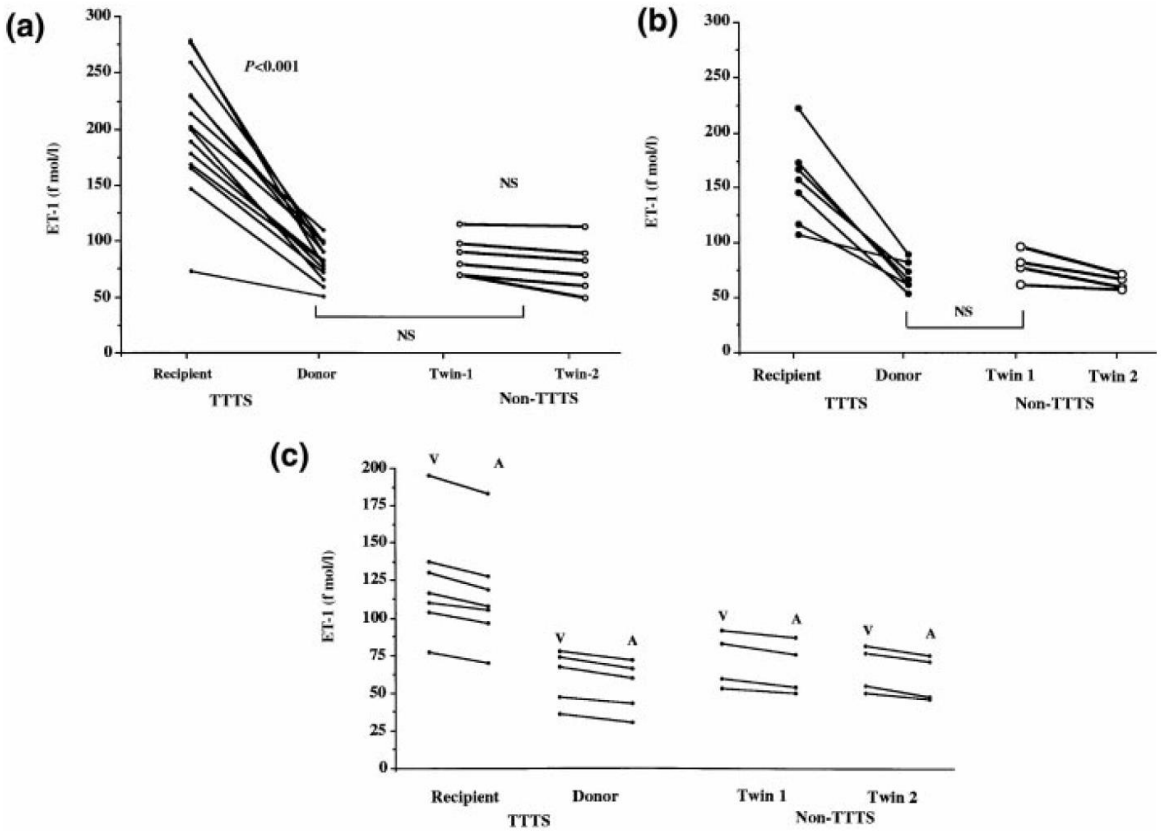


Figure 1. Endothelin (ET-1) concentrations in monochorionic twins with or without twin–twin transfusion syndrome (TTTS) (**a**) at the time of fetal blood sampling *in utero*; (**b**) in amniotic fluid, and (**c**) in umbilical vein (V) and artery (A) at the time of delivery. NS = non-significant.

Bajoria R, Sullivan M, Fisk NM. Endothelin concentrations in monochorionic twins with severe twin-twin transfusion syndrome. Hum Reprod. 1999 Jun;14(6):1614-8.

Fisiopatología

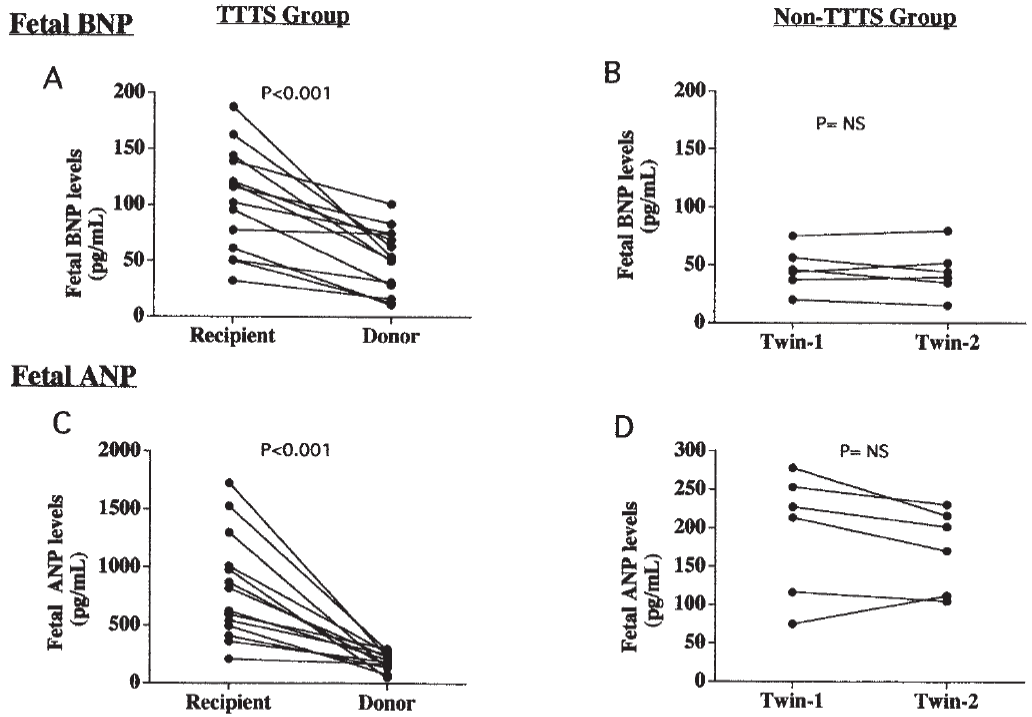


Fig 1. Comparison of fetal brain natriuretic peptide (BNP) levels in utero between (**A**) recipient and donor twins with chronic twin-twin transfusion syndrome (TTTS) and (**B**) monochorionic twin pairs without chronic TTTS. **C** and **D** compare fetal atrial natriuretic peptide (ANP) levels in utero between twin pairs with and without chronic TTTS, respectively.

Bajoria R, Ward S, Chatterjee R. Natriuretic peptides in the pathogenesis of cardiac dysfunction in the recipient fetus of twin-twin transfusion syndrome. Am J Obstet Gynecol. 2002 Jan;186(1):121-7.

Fisiopatología

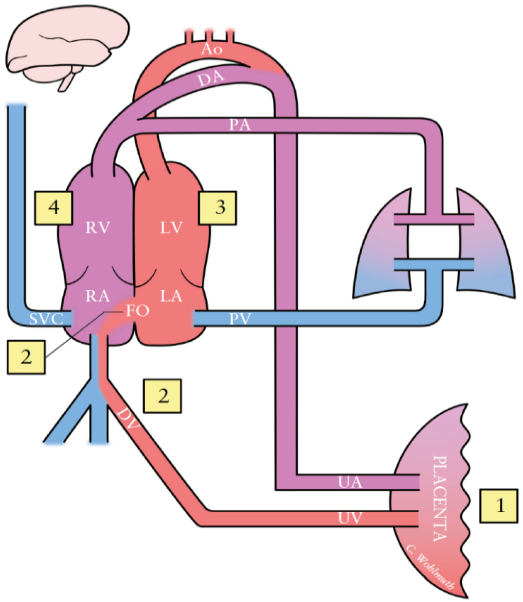


Figure 3 Proposed pathophysiology of recipient twin in twin–twin transfusion syndrome. (1) Neuroendocrine factors cause increased recipient blood pressure. (2) Decreased right-to-left shunting and altered ductus venosus (DV) filling times are observed. (3) Altered left ventricular (LV) function and, ultimately, (4) bilateral atrioventricular valve regurgitation and ventricular hypertrophy are seen. Ao, aorta; DA, ductus arteriosus; FO, foramen ovale; LA, left atrium; PA, pulmonary arteries; PV, pulmonary veins; RA, right atrium; RV, right ventricle; SVC, superior vena cava; UA, umbilical artery; UV, umbilical vein.

1.- Factores neuroendocrinos aumentan presión arterial en el receptor.

2.- Disminuye el shunt derecha-izquierda y se altera el ductus venoso.

3.- Se altera la función del ventrículo izquierdo

4.- Regurgitación en ambas válvulas AV e hipertrofia ventricular

Wohlmuth C, Boudreaux D, Moise KJ Jr, Johnson A, Papanna R, Bebbington M, Gardiner HM. Cardiac pathophysiology in twin-twin transfusion syndrome: new insights into its evolution. Ultrasound Obstet Gynecol. 2018 Mar;51(3):341-348.

Clasificación STFF

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TABLE 1

Quintero Staging of TTTS is the Established Framework for Staging TTTS

Stage I	Donor bladder visible
Stage II	No donor bladder Normal Doppler assessments
Stage III	Abnormal Doppler assessments For donor: -AEDF/REDF in donor umbilical artery +/- For recipient: -Abnormal DV flow -Pulsatile umbilical vein
Stage IV	Hydrops in one twin
Stage V	Death of one/both twins

Note: AEDF; absent end diastolic flow; REDF: reversed end diastolic flow; DV: ductus venosus.

TABLE 2

Quantifiable Functional Changes in the Recipient Twin

1	Ventricular myocardial hypertrophy	• Right ventricle before left • Both ventricles in time
2	Increased heart size	• Hypertrophy not dilatation • Increased C:T ratio
3	Ventricular hypokinesia	• Increased MPI
4	Atrioventricular valvar dysfunction	• Regurgitation • TV before MV • Monophasic inflow
5	+/- RVOTO	• Acceleration across the RVOT • Pulmonary regurgitation

Note: C:T ratio = cardiothoracic; TV = tricuspid valve; MV = mitral valve; RVOT = Right ventricular outflow tract.

Manning N, Archer N. Cardiac Manifestations of Twin-to-Twin Transfusion Syndrome. Twin Res Hum Genet. 2016 Jun;19(3):246-54.

TABLE 4

Possible Mechanisms for the Development of Acquired Structural Heart Disease

	Right ventricular outflow tract obstruction in recipient	Coarctation of the aorta in the donor
	Right ventricular (RV) myocardial hypertrophy	High placental resistance
	Reduced RV function + high systemic pressures	+ Hypovolaemia
	+/- Severe tricuspid regurgitation	Decreased venous return from placenta → Reduced anterograde flow from left ventricle across aortic isthmus
	Inability of the RV to generate enough pressure to open pulmonary valve	Reduced growth of arch
	Progression to muscular (subvalvar) and valvar RVOTO	Evolving coarctation

Manning N, Archer N. Cardiac Manifestations of Twin-to-Twin Transfusion Syndrome. Twin Res Hum Genet. 2016 Jun;19(3):246-54.

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American Journal of Obstetrics and Gynecology (2005) **192**, 892–902

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American Journal of OBSTETRICS and GYNECOLOGY
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Prenatal cardiovascular manifestations in the twin-to-twin transfusion syndrome recipients and the impact of therapeutic amnioreduction

Catherine Barrea, MD,[a] Fawaz Alkazaleh, MD,[b] Greg Ryan, MB,[b] Brian W. McCrindle, MD,[a] Anita Roberts, BSc,[a] Jean-Luc Bigras, MD,[a] Jon Barrett, MD,[c] Gareth P. Seaward, MB,[b] Jeffrey F. Smallhorn, MB, BS,[a] Lisa K. Hornberger, MD[a,*]

Department of Pediatrics, Division of Cardiology, Fetal Cardiac Program, The Hospital for Sick Children,[a] and the Division of Maternal-Fetal Medicine, Mount Sinai Hospital[b] and Women's College Hospital,[c] University of Toronto, Ontario, Canada

Table II Diastolic dysfunction in the recipient twin at examination (n = 28 recipients)

Variable	Proportion (n/N)
Diastolic dysfunction	16/24 (67%)
Abnormal IVC/hepatic vein blood flow	13/20 (65%)
Abnormal ductus venosus blood flow	7/14 (50%)
Umbilical vein pulsations	9/22 (41%)
Abnormal mitral valve blood inflow	8/21 (38%)
Abnormal tricuspid valve blood inflow	12/20 (60%)
Abnormal LV isovolumic contraction time	11/18 (61%)

Barrea C, Alkazaleh F, Ryan G, McCrindle BW, Roberts A, Bigras JL, Barrett J, Seaward GP, Smallhorn JF, Hornberger LK. Prenatal cardiovascular manifestations in the twin-to-twin transfusion syndrome recipients and the impact of therapeutic amnioreduction. Am J Obstet Gynecol. 2005 Mar;192(3):892-902.

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Table III The cardiovascular findings at examination, according to the staging of Quintero et al[22]

Finding	Stage			
	I-II	III	IV	*P* value
Total recipients (n)	7	17	4	
RVSF (%)*	30 ± 9	33 ± 13	21 ± 8	NS
RVSF <28% (n/N)	1/7 (14%)	5/15 (33%)	3/4 (75%)	NS
LVSF (%)*	40 ± 11	39 ± 10	28 ± 5	NS
LVSF <28% (n/N)	0/7 (0%)	2/16 (13%)	2/4 (50%)	NS
Moderate to severe tricuspid valve regurgitation (n/N)	0/5 (0%)	3/17 (18%)	4/4 (100%)	.004
Moderate to severe mitral valve regurgitation (n/N)	0/5 (0%)	0/17 (0%)	3/4 (75%)	.002
Diastolic dysfunction (n/N)	3/6 (50%)	9/14 (64%)	4/4 (100%)	NS
RV anterior wall thickness (Z score)*	+1.46 ± 1.39	+1.98 ± 1.53	+3.43 ± 1.54	NS
Interventricular wall thickness (Z score)*	+1.70 ± 0.87	+2.20 ± 1.22	+2.52 ± 0.53	NS
LV posterior wall thickness (Z score)*	+1.67 ± 1.53	+1.74 ± 1.59	+3.31 ± 0.60	NS
Right and/or left hypertrophy (n/N)	2/7 (29%)	9/15 (60%)	4/4 (100%)	.077

NS, Not statistically significant ($P \geq 1.0$).
* Data are given as mean ± SD.

Barrea C, Alkazaleh F, Ryan G, McCrindle BW, Roberts A, Bigras JL, Barrett J, Seaward GP, Smallhorn JF, Hornberger LK. Prenatal cardiovascular manifestations in the twin-to-twin transfusion syndrome recipients and the impact of therapeutic amnioreduction. Am J Obstet Gynecol. 2005 Mar;192(3):892-902.

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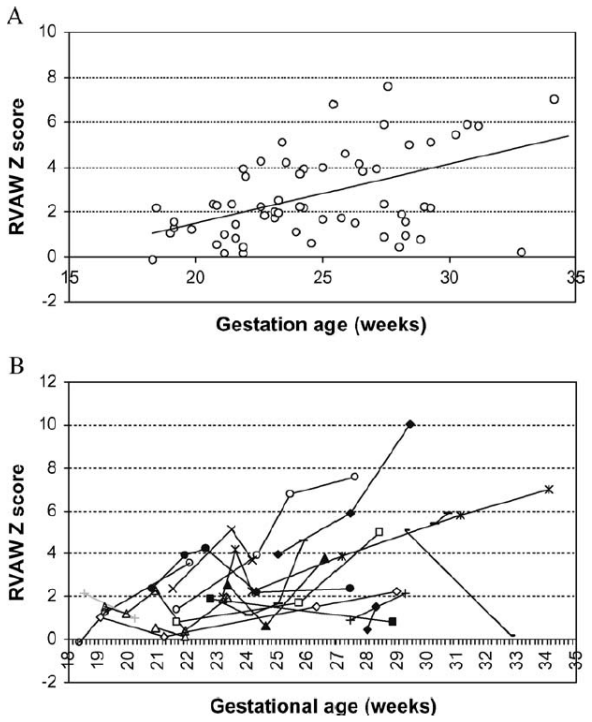

Figure 3 The progression of right ventricular hypertrophy (RVAW thickness normalized for GA and expressed in Z score) in fetuses that were assessed serially after amnioreductions. **A,** Graph shows a regression curve for all measures; **B**, graph shows individual measurements for each fetus that was assessed. Similar progression was observed for the interventricular septum and the left ventricular posterior wall (results not shown).

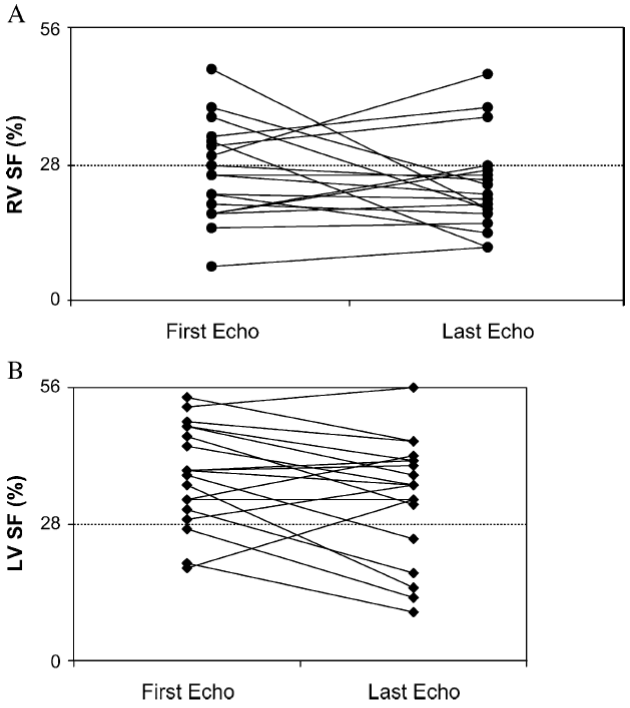

Figure 4 The changes in RVSF (**A**) and LVSF (**B**) between the first and the last postamnioreduction echocardiogram, respectively, that was performed in 19 recipients. RV systolic function remained (10/19) or became (5/19) abnormal (SF, <28%) in 79% and normalized in only 1 recipient, despite amnioreduction, whereas LV systolic function remained (13/19) or became (1/19) normal (SF, ≥28%) in 74% and became abnormal (SF, <28%) in 3 cases.

Barrea C, Alkazaleh F, Ryan G, McCrindle BW, Roberts A, Bigras JL, Barrett J, Seaward GP, Smallhorn JF, Hornberger LK. Prenatal cardiovascular manifestations in the twin-to-twin transfusion syndrome recipients and the impact of therapeutic amnioreduction. Am J Obstet Gynecol. 2005 Mar;192(3):892-902.

Cardiopatía en STFF

American Journal of Obstetrics and Gynecology (2006) **195**, 1388–95

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American Journal of Obstetrics & Gynecology
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Impact of selective laser ablation of placental anastomoses on the cardiovascular pathology of the recipient twin in severe twin-twin transfusion syndrome

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Table I Demographic data for the 35 pregnancies assessed by fetal echocardiography

	Subgroup with echo pre and post (n = 22)	Subgroup with echo pre only (n = 13)	*P* value
Maternal age (years)	31 ± 5	29 ± 5	NS
GA at presentation (weeks)	19.4 ± 2.8	19.2 ± 2.2	NS
GA at laser (weeks)	21.7 ± 2.6	21.3 ± 2.8	NS
Number of anastomoses ablated	10 ± 3	11 ± 5	NS
Volume of amnioreduction (liters)	2.3 ± 1.4	2.1 ± 0.8	NS
GA at delivery (weeks)	31.9 ± 4.5	28.9 ± 6.6	NS
TTTS stage:			
Stage 1	0	1	
Stage 2	1	3	
Stage 3	16	8	
Stage 4	5	1	

Demographic data, laser procedure characteristics, and GA at delivery expressed as mean ± SD. Comparisons were made between the two subgroups with an unpaired student's *t* test. *GA*, Gestational age.

Barrea C, Hornberger LK, Alkazaleh F, McCrindle BW, Roberts A, Berezovska O, Windrim R, Seaward PG, Smallhorn JF, Ryan G. Impact of selective laser ablation of placental anastomoses on the cardiovascular pathology of the recipient twin in severe twin-twin transfusion syndrome. Am J Obstet Gynecol. 2006 Nov;195(5):1388-95.

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Table II Cardiovascular findings among recipient twins before and acutely after the laser procedure

	n	Pre-laser	Post-laser	*P* value
Gestational age (weeks)	22	21.4 ± 2.7	22.4 ± 2.4	NS
Fetal heart rate (bpm)	16	144 ± 9	143 ± 5	NS
Cardiothoracic ratio	18	0.50 ± 0.09	0.51 ± 0.11	NS
Z score RVED	21	−0.70 ± 1.00	−0.57 ± 0.68	NS
Z score LVED	21	−0.58 ± 0.77	−0.54 ± 0.77	NS
Z score LVPW	18	+2.09 ± 1.98	+1.68 ± 1.75	NS
Z score RVAW	18	+1.83 ± 1.95	+1.84 ± 1.64	NS
Z score IVS	17	+2.16 ± 1.64	+2.16 ± 1.26	NS
Systolic function				
RVSF (%)	22	25 ± 12	32 ± 9	0.007
LVSF (%)	22	32 ± 9	36 ± 7	0.04
RVSF <28%	22	13 (59%)	8 (36%)	< 0.03
LVSF <28%	22	6 (27%)	2 (9%)	0.1
Moderate to severe TR	22	9 (41%)	4 (18%)	0.03
Moderate to severe MR	22	6 (27%)	3 (14%)	NS
Diastolic dysfunction				
(≥2 abnormal parameters)	22	16 (73%)	11 (50%)	0.06
Abnormal IVC flow	20	14 (70%)	14 (70%)	NS
Abnormal DV flow	16	13 (81%)	9 (56%)	< 0.05
UV pulsations	18	16 (89%)	9 (50%)	0.008
Abnormal LV IVRT	17	9 (53%)	6 (35%)	NS
LV IVRT (msec)	17	58 ± 9	54 ± 8	0.048
Abnormal TV flow	13	11 (85%)	3 (23%)	0.005
Abnormal MV flow	16	6 (38%)	1 (6%)	0.06
RV Tei ratio	10	1.41 ± 0.34	1.00 ± 0.22	0.03
LV Tei ratio	17	0.99 ± 0.33	0.90 ± 0.24	NS

The results are expressed as mean ± SD or the absolute number with percentage in parens. The Tei index is expressed as a ratio of the actual value divided by the normal value for gestational age, as such a perfectly normal value = 1. Statistical analyses were done by paired student's *t* test for continuous variables and by McNemar test for proportions. *bpm*, Beats per minute; *DV*, ductus venosus; *IVC*, inferior vena cava; *IVS*, interventricular septum thickness; *LVED*, left ventricular end-diastolic diameter; *LV IVRT*, left ventricular isovolumic relaxation time in milliseconds; *LVPW*, left ventricular posterior wall thickness; *LVSF*, left ventricular shortening fraction; *MV*, mitral valve; *MR*, mitral regurgitation; *RVAW*, right ventricular anterior wall thickness; *RVED*, right ventricular end-diastolic diameter; *RVSF*, right ventricular shortening fraction; *TV*, tricuspid valve; *TR*, tricuspid regurgitation.

Barrea C, Hornberger LK, Alkazaleh F, McCrindle BW, Roberts A, Berezovska O, Windrim R, Seaward PG, Smallhorn JF, Ryan G. Impact of selective laser ablation of placental anastomoses on the cardiovascular pathology of the recipient twin in severe twin-twin transfusion syndrome. Am J Obstet Gynecol. 2006 Nov;195(5):1388-95.

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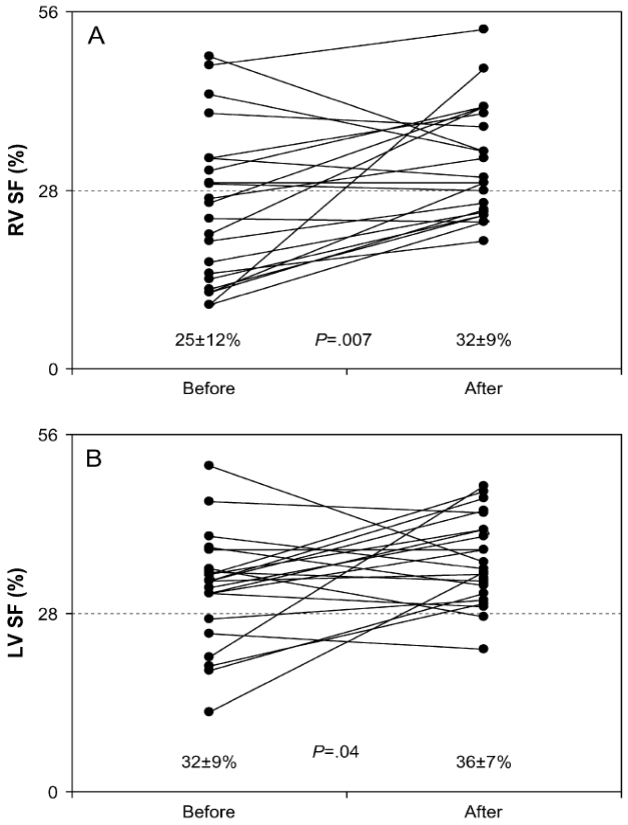

Figure 1 This graph demonstrates the changes in **A**, right (RV) and **B**, left ventricular (LV) shortening fraction (SF) immediately before and after laser.

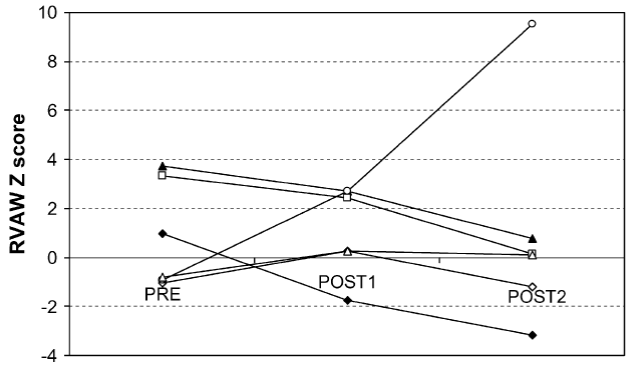

Figure 3 This graph shows the evolution of right ventricular anterior wall thickness (RVAW) *Z* score just before the laser (PRE), at the first echo after the procedure (POST1), and at late follow-up (POST2). There was no progression of wall thickness after the laser except for one case in which there was evidence of ongoing twin-twin transfusion syndrome despite ablation of multiple anastomoses. Similar observations were made for the interventricular septum and LV posterior wall thickness (results not shown).

Barrea C, Hornberger LK, Alkazaleh F, McCrindle BW, Roberts A, Berezovska O, Windrim R, Seaward PG, Smallhorn JF, Ryan G. Impact of selective laser ablation of placental anastomoses on the cardiovascular pathology of the recipient twin in severe twin-twin transfusion syndrome. Am J Obstet Gynecol. 2006 Nov;195(5):1388-95.

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The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease

Jack Rychik, MD; Zhiyun Tian, MD; Michael Bebbington, MD; Feng Xu, MD; Margaret McCann, BA; Stephanie Mann, MD; R. Douglas Wilson, MD; Mark P. Johnson, MD

Rychik J, Tian Z, Bebbington M, Xu F, McCann M, Mann S, Wilson RD, Johnson MP. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. Am J Obstet Gynecol. 2007 Oct;197(4):392.e1-8.

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TABLE 1
Cardiovascular parameters that were used to make up the CV Score and the number of fetuses with specific cardiovascular findings

Variable	Parameter	Finding	Numeric score	Fetuses with this finding (n)
Donor	Umbilical artery	Normal	0	96 (64%)
		Decreased diastolic blood flow	1	34 (23%)
		Absent/reversed diastolic blood flow	2	20 (13%)
Recipient	Ventricular hypertrophy	None	0	77 (51%)
		Present	1	73 (49%)
	Cardiac dilation	None	0	78 (52%)
		Mild	1	47 (31%)
		>mild	2	25 (17%)
	Ventricular dysfunction	None	0	117 (78%)
		Mild	1	12 (8%)
		>mild	2	21 (14%)
	Tricuspid valve regurgitation	None	0	97 (65%)
		Mild	1	31 (21%)
		>mild	2	22 (15%)
	Mitral valve regurgitation	None	0	131 (87%)
		Mild	1	6 (4%)
		>mild	2	13 (9%)
	Tricuspid valve inflow	Double-peak	0	113 (75%)
		Single-peak	1	37 (25%)
	Mitral valve inflow	Double-peak	0	135 (90%)
		Single-peak	1	15 (10%)
	Ductus venosus	All antegrade	0	114 (76%)
		Absent diastolic blood flow	1	13 (9%)
		Reverse diastolic blood flow	2	23 (15%)
	Umbilical vein	No pulsations	0	136 (91%)
		Pulsations	1	14 (9%)
	Right-sided outflow tract	Pulmonary artery > aorta	0	126 (84%)
		Pulmonary artery = aorta	1	13 (9%)
		Pulmonary artery < aorta	2	8 (5%)
		Right ventricle outflow obstruction	3	3 (2%)
	Pulmonary regurgitation	None	0	145 (97%)
		Present	1	5 (3%)

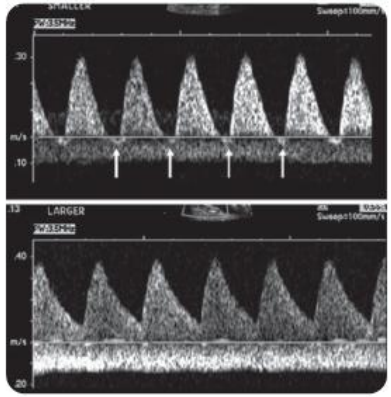
CV 1 0-5
CV 2 6-10
CV 3 11-15
CV 4 16-20

Rychik J, Tian Z, Bebbington M, Xu F, McCann M, Mann S, Wilson RD, Johnson MP. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. Am J Obstet Gynecol. 2007 Oct;197(4):392.e1-8.

Cardiopatía en STFF

FIGURE 1

Doppler spectral display of umbilical arterial and venous flow in the donor (top panel) and recipient (bottom panel) twins

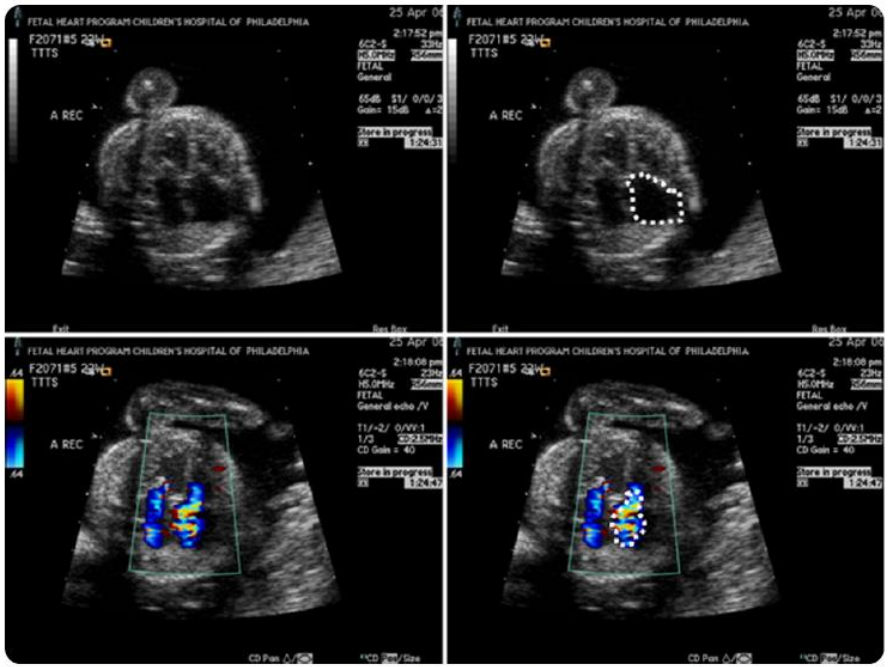


Arrows point to the reversal of diastolic blood flow that was noted in the donor twin as arterial blood flow below the baseline. Umbilical venous blood flow is continuous and nonphasic, all below the baseline.

Rychik. The twin-to-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. AJOG 2007.

FIGURE 2

Severe tricuspid and mitral regurgitation in a recipient twin heart



Top panels are the 2-dimensional images of a 4-chamber view; **bottom panels** are the color Doppler images that show valve regurgitation. The **right-side panels** show tracings of the area of right atrium (*top*) and the area of the color regurgitant jet (*bottom*). Note that the color jet regurgitant area is much >25% of the right atrial area, which designates this as hemodynamically significant (more than mild) tricuspid regurgitation.

Rychik. The twin-to-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. AJOG 2007.

Rychik J, Tian Z, Bebbington M, Xu F, McCann M, Mann S, Wilson RD, Johnson MP. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. Am J Obstet Gynecol. 2007 Oct;197(4):392.e1-8.

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FIGURE 3

Doppler spectral display of inflow pattern across the tricuspid valve

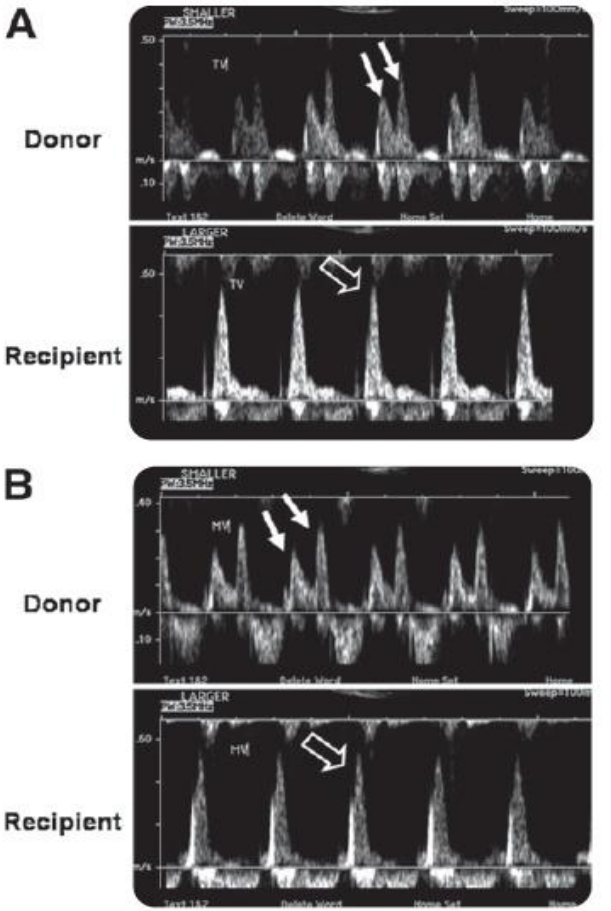
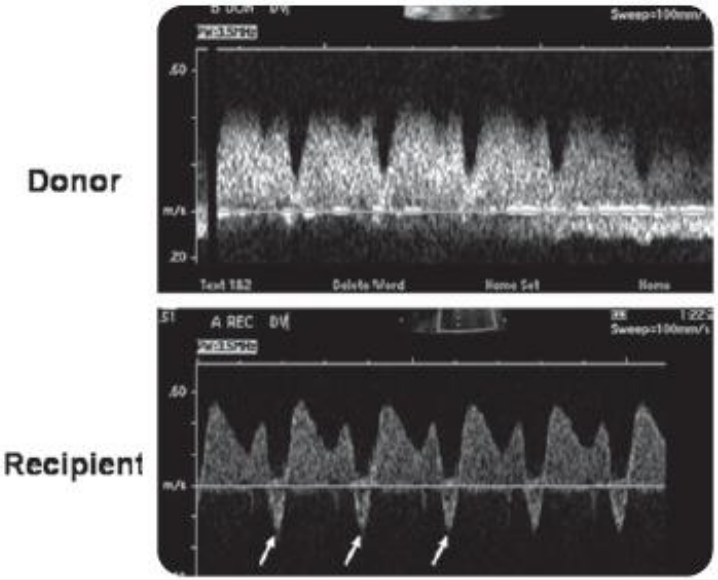


FIGURE 4

Doppler spectral display of flow in the ductus venosus



Rychik J, Tian Z, Bebbington M, Xu F, McCann M, Mann S, Wilson RD, Johnson MP. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. Am J Obstet Gynecol. 2007 Oct;197(4):392.e1-8.

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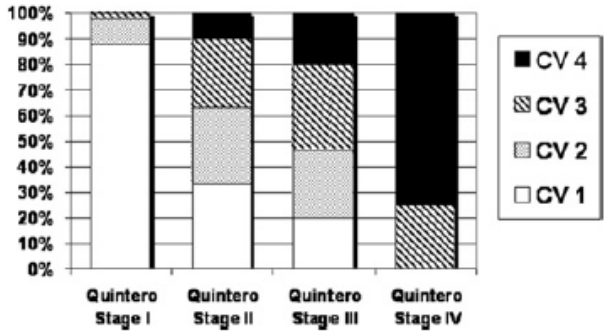
TABLE 4
Quantitative parameters of cardiovascular function evaluated in both the donor and recipient fetuses

Parameter	Donor	Recipient	*P* value
Weight (g)	399 (235)	527 (285)	<.0001
Umbilical artery			
S wave peak velocity (cm/s)	29.2 (8.7)	41.7 (12.9)	<.0001
D wave peak velocity (cm/s)	4.7 (4.3)	9.7 (4.5)	<.0001
Pulsatility index	1.81 (0.8)	1.46 (0.4)	<.0001
Middle cerebral artery			
S wave peak velocity (cm/s)	27.3 (8.1)	26.2 (8)	NS
D wave peak velocity (cm/s)	5.1 (2.6)	5.1 (2.1)	NS
Pulsatility index	1.79 (0.4)	1.70 (0.4)	NS
Ductus venosus			
A wave peak velocity (cm/s)	18.5 (6.8)	13.3 (16.7)	<.01
S wave peak velocity (cm/s)	51.1 (13)	53.3 (13.6)	NS
A/S ratio	0.38 (0.12)	0.24 (0.31)	<.001
Tricuspid valve closure-to-opening time (msec)	232 (18)	275 (32)	<.0001
Pulmonary artery ejection time (msec)	169 (13)	169 (21)	NS
Right ventricle myocardial performance index (Tei Index)	0.38 (0.11)	0.69 (0.47)	<.0001
Mitral valve closure-to-opening time (msec)	222 (19)	263 (29)	<.0001
Aorta ejection time (msec)	166 (15)	170 (17)	.07
Left ventricle myocardial performance index (Tei Index)	0.34 (0.12)	0.59 (0.28)	<.0001

FIGURE 6
Bar graph shows the percentage of twin pairs with a particular cardiovascular grade for each Quintero stage



Note the presence of significant discrepancy in categorization of severity in particular for Quintero stages II and II, in which a wide variety of cardiovascular grades are found.

Rychik. The twin-to-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. AJOG 2007.

Rychik J, Tian Z, Bebbington M, Xu F, McCann M, Mann S, Wilson RD, Johnson MP. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. Am J Obstet Gynecol. 2007 Oct;197(4):392.e1-8.

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Ultrasound Obstet Gynecol 2018; **51**: 341–348
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Cardiac pathophysiology in twin–twin transfusion syndrome: new insights into its evolution

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Table 3 Calculated cardiac output in 26 uncomplicated monochorionic–diamniotic (MCDA) pregnancies and 119 pregnancies complicated by Stages I and II or Stages III and IV twin–twin transfusion syndrome (TTTS)

	Uncomplicated (n = 26)			*TTTS I+II* (n = 61)			*TTTS III+IV* (n = 58)		
Parameter	*Larger twin*	*Smaller twin*	P	*Recipient*	*Donor*	P	*Recipient*	*Donor*	P
Left cardiac output (mL/min/kg)	209 ± 129	158 ± 51	0.091	168 ± 49	157 ± 64	0.205	190 ± 58	149 ± 61	0.001
Right cardiac output (mL/min/kg)	301 ± 225	259 ± 87	0.568	244 ± 74	233 ± 86	0.328	235 ± 119	233 ± 85	0.783
Combined cardiac output (mLmin/kg)	510 ± 260	417 ± 89	0.101	411 ± 95	376 ± 135	0.182	423 ± 140	381 ± 119	0.088

Data are given as mean ± SD of left, right and combined cardiac output, normalized to estimated fetal weight.

Wohlmuth C, Boudreaux D, Moise KJ Jr, Johnson A, Papanna R, Bebbington M, Gardiner HM. Cardiac pathophysiology in twin-twin transfusion syndrome: new insights into its evolution. Ultrasound Obstet Gynecol. 2018 Mar;51(3):341-348.

Table 2 Basic cardiovascular parameters in 26 uncomplicated monochorionic–diamniotic (MCDA) pregnancies and 119 pregnancies complicated by Stages I and II or Stages III and IV twin–twin transfusion syndrome (TTTS)

Parameter	*Uncomplicated MCDA (n = 26)*	*TTTS I+II (n = 61)*	*TTTS III+IV (n = 58)*
TTTS recipient/larger MCDA twin			
HR (bpm)	145 ± 7	144 ± 7	142 ± 8
TV E/A ratio	0.64 ± 0.10	0.62 ± 0.12	0.65 ± 0.16
TV E/A fusion	4 (15.4)	16 (26.2)	20 (34.5)
Tricuspid regurgitation	4 (15.4)	14 (23.0)	29 (50.0)
Mild	4 (15.4)	9 (14.8)	12 (20.7)
Moderate–severe	—	5 (8.2)	17 (29.3)
MV E/A ratio	0.64 ± 0.09	0.61 ± 0.10	0.60 ± 0.11
MV E/A fusion	—	5 (8.2)	6 (10.3)
Mitral regurgitation	—	3 (4.9)	16 (27.6)
Mild	—	1 (1.6)	7 (12.1)
Moderate–severe	—	2 (3.3)	9 (15.5)
DA reverse flow	—	—	5 (8.6)
UA-PI	1.32 ± 0.19	1.34 ± 0.27	1.82 ± 0.97
UA-AREDF	—	—	6 (10.3)
DV-AREDF	—	—	23 (39.7)
UV pulsations	—	—	21 (36.2)
MCA-PSV MoM	1.2 ± 0.2	1.0 ± 0.2	1.0 ± 0.2
TTTS donor/smaller MCDA twin			
HR (bpm)	148 ± 9	147 ± 10	147 ± 10
TV E/A ratio	0.69 ± 0.07	0.67 ± 0.11	0.69 ± 0.10
TV E/A fusion	—	—	—
Tricuspid regurgitation	—	5 (8.2)	2 (3.4)
Mild	—	5 (8.2)	2 (3.4)
Moderate–severe	—	—	—
MV E/A ratio	0.71 ± 0.30	0.66 ± 0.13	0.67 ± 0.13
MV E/A fusion	—	—	—
Mitral regurgitation	—	—	—
Mild	—	—	—
Moderate–severe			
UA-PI	1.33 ± 0.22	1.43 ± 0.34	1.94 ± 0.83
UA-AREDF	—	—	19 (32.8)
DV-AREDF	—	—	9 (15.5)
UV pulsations	—	—	9 (15.5)
MCA-PSV MoM	1.1 ± 0.2	1.2 ± 0.3	1.3 ± 0.4

Data are given as mean ± SD or *n* (%). AREDF, absent or reversed end-diastolic flow; bpm, beats per minute; DA, ductus arteriosus; DV, ductus venosus; E/A, fusion of passive (E) and active (A) ventricular filling waves; HR, heart rate; MCA-PSV, middle cerebral artery peak systolic velocity; MoM, multiples of the median; MV, mitral valve; PI, pulsatility index; TV, tricuspid valve; UA, umbilical artery; UV, umbilical vein.

Wohlmuth C, Boudreaux D, Moise KJ Jr, Johnson A, Papanna R, Bebbington M, Gardiner HM. Cardiac pathophysiology in twin-twin transfusion syndrome: new insights into its evolution. Ultrasound Obstet Gynecol. 2018 Mar;51(3):341-348.

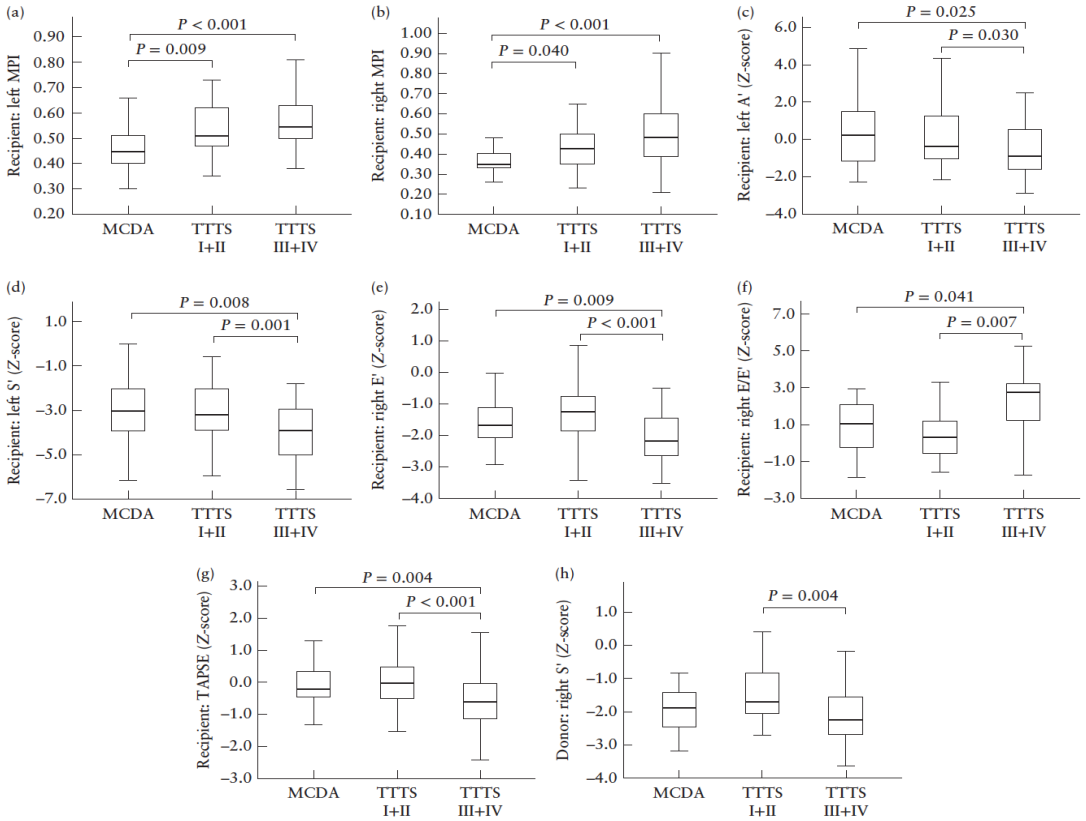

Figure 1 Box-and-whiskers plots comparing left (a) and right (b) myocardial performance index (MPI), left tissue Doppler-derived velocities during late diastole (A′) (c) and systole (S′) (d), right tissue Doppler velocity during early diastole (E′) (e), transtricuspid-to-tricuspid annular velocity ratio (E/E′) (f) and tricuspid annular plane systolic excursion (TAPSE) (g) of recipient cotwins, as well as right tissue Doppler-derived velocity during systole (S′) of donor cotwins (h), in pregnancies complicated by Stages I and II (TTTS I+II) or Stages III and IV (TTTS III+IV) twin–twin transfusion syndrome and uncomplicated monochorionic–diamniotic (MCDA) pregnancies. Boxes show median and interquartile range, and whiskers are range.

Wohlmuth C, Boudreaux D, Moise KJ Jr, Johnson A, Papanna R, Bebbington M, Gardiner HM. Cardiac pathophysiology in twin-twin transfusion syndrome: new insights into its evolution. Ultrasound Obstet Gynecol. 2018 Mar;51(3):341-348.

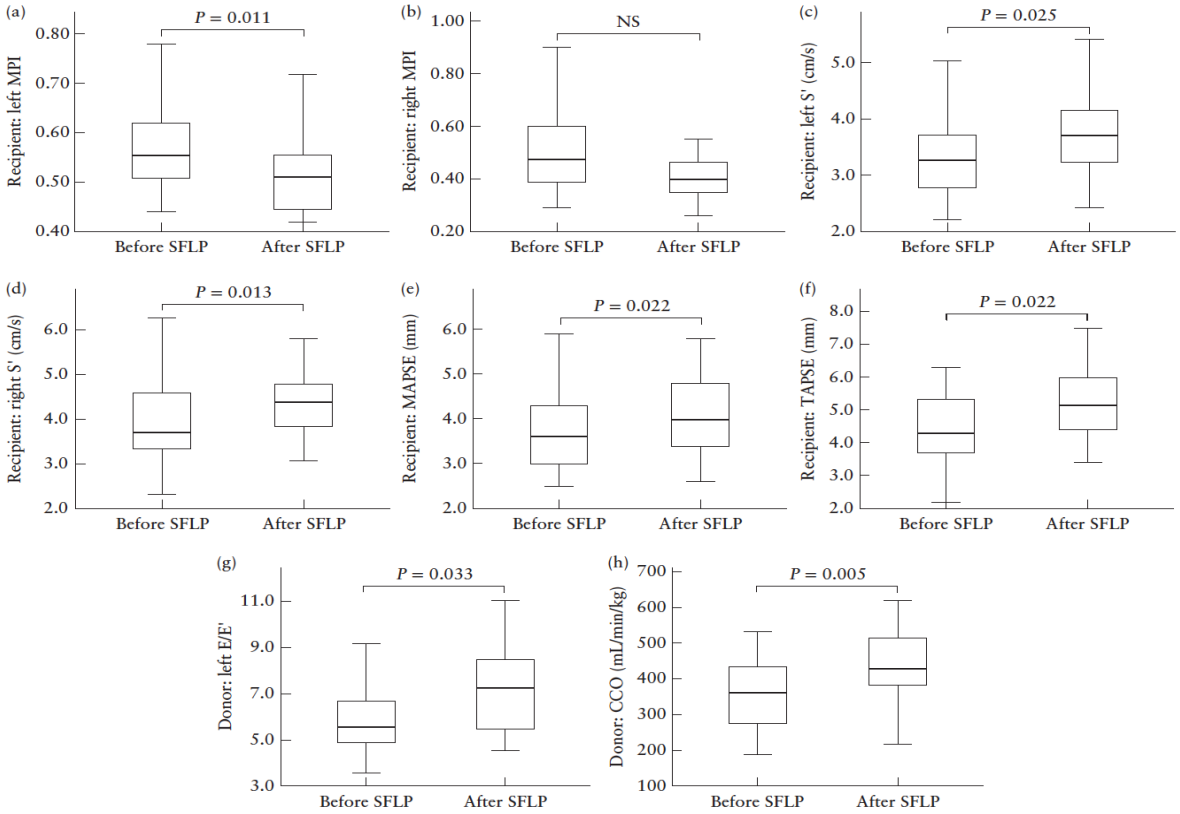

Figure 2 Box-and-whiskers plots comparing left (a) and right (b) myocardial performance index (MPI), left (c) and right (d) tissue Doppler-derived velocities during systole (S′) and mitral (MAPSE) (e) and tricuspid (TAPSE) (f) annular plane systolic excursion of recipient cotwin, as well as transmitral-to-mitral annular velocity ratio (E/E′) (g) and combined cardiac output (CCO) (h) of donor cotwin, in 41 pregnancies complicated by twin–twin transfusion syndrome, before and after selective fetoscopic laser photocoagulation (SFLP). Boxes show median and interquartile range and whiskers are range. NS, not significant.

Wohlmuth C, Boudreaux D, Moise KJ Jr, Johnson A, Papanna R, Bebbington M, Gardiner HM. Cardiac pathophysiology in twin-twin transfusion syndrome: new insights into its evolution. Ultrasound Obstet Gynecol. 2018 Mar;51(3):341-348.

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Journal of Paediatrics and Child Health

doi:10.1111/j.1440-1754.2009.01641.x

ORIGINAL ARTICLE

Twin–twin transfusion syndrome, coarctation of the aorta and hypoplastic aortic arch: A case series report

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[1]Newborn Service, Auckland City Hospital, [2]Departments of Paediatrics and Obstetrics and Gynaecology, University of Auckland and [3]Department of Paediatric Cardiology, Starship Hospital, Auckland, New Zealand

Table 1 Overview of demographics, main (cardiac) diagnoses and outcome of the twin pairs

	Gender	Gestation (weeks)	Birthweight (g)	Diagnosis	Outcome
Twin 1	Female	27	1200	PPHN	Death
Twin 2	Female	27	725	PDA, coarctation	Persistent neurological problems
Twin 1	Male	28	1180	CLD, PDA	Discharged
Twin 2	Male	28	850	RDS, PDA, coarctation	Discharged
Twin 1	Female	25	713	CLD, coarctation	Discharged
Twin 2	Female	25	937	Dysplastic aortic valves, LV hypertrophy, severe MR	Death
Twin 1	Male	33	1520	Coarctation, PDA, cystic PVL	Transferred to referring hospital
Twin 2	Male	33	2490	PPHN, Ebstein's anomaly	Transferred to referring hospital

CLD, chronic lung disease; LV, left ventricle; MR, mitral regurgitation; PDA, persistent ductus arteriosus; PPHN, persistent pulmonary hypertension of the newborn; PVL, periventricular leucomalacia; RDS, respiratory distress syndrome; VSD, ventricular septal defect.

van den Boom J, Battin M, Hornung T. Twin-twin transfusion syndrome, coarctation of the aorta and hypoplastic aortic arch: a case series report. J Paediatr Child Health. 2010 Mar;46(3):76-9.

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Right ventricular outflow tract obstruction (RVOTO)

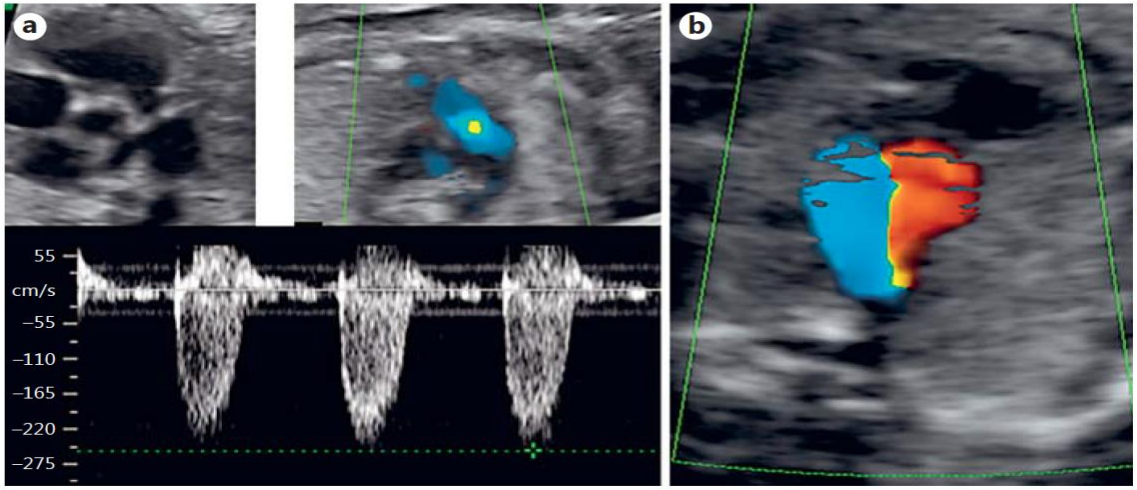

Fig. 1. Echocardiographic diagnostic criteria. **a** PS (thickened or narrow pulmonary valve, turbulent flow, peak systolic velocity >120 cm/s). **b** PA (no forward flow across the pulmonary valve, reverse flow in the ductus arteriosus).

Ortiz JU, Masoller N, Gómez O, Bennasar M, Eixarch E, Lobmaier SM, Crispi F, Gratacos E, Martinez JM. Rate and Outcomes of Pulmonary Stenosis and Functional Pulmonary Atresia in Recipient Twins with Twin-Twin Transfusion Syndrome. Fetal Diagn Ther. 2017;41(3):191-196.

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Table 2. Definitions of Anatomic Subtype and Post-SFLP Improvement in RVOT Abnormalities

	Pulmonary Atresia	Pulmonary Stenosis	Isolated Pulmonary Insufficiency
Anatomic findings	Functional: none–minimal antegrade flow across RVOT, PI present, exclusive retrograde flow in DA Anatomic: no antegrade flow across RVOT, no PI present	Turbulent, accelerated flow across anatomically thickened/dysplastic pulmonary valve or narrowed RVOT	Pulmonary insufficiency in absence of RVOT obstruction
Post-SFLP improvement	Appearance of improved antegrade flow across RVOT and/or: Change to normal antegrade flow across DA	20% decrement in flow velocity across RVOT	Resolution of pulmonary insufficiency

DA, ductus arteriosus; PI, pulmonary insufficiency; RVOT, right ventricular outflow tract; SFLP, selective fetoscopic laser procedure.

Michelfelder E, Tan X, Cnota J, Divanovic A, Statile C, Lim FY, Crombleholme T. Prevalence, Spectrum, and Outcome of Right Ventricular Outflow Tract Abnormalities in Twin-twin Transfusion Syndrome: A Large, Single-center Experience. Congenit Heart Dis. 2015 May-Jun;10(3):209-18.

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Table 4. Published Reports on the *Prenatal* Prevalence of RVOT Abnormalities in Twin–twin Transfusion Syndrome

Author	Year	Subjects (n)	Prevalence of RVOT Abnormality (%)
Lougheed et al.[9]	2001	48	6/48 (12.5)
Barrea et al.[10]	2005	28	4/28 (14.3)
Michelfelder et al.[11]	2007	42	5/42 (11.9)
Moon-Grady et al.[15]	2011	76	16/76 (21.0)
Current study	N/A	610	53/610 (8.7)

RVOT, right ventricular outflow tract.

Michelfelder E, Tan X, Cnota J, Divanovic A, Statile C, Lim FY, Crombleholme T. Prevalence, Spectrum, and Outcome of Right Ventricular Outflow Tract Abnormalities in Twin-twin Transfusion Syndrome: A Large, Single-center Experience. Congenit Heart Dis. 2015 May-Jun;10(3):209-18.

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Table 3. Echocardiographic Findings in Three Subgroups with Right Ventricular Outflow Tract Abnormalities in Recipient Twins

		PA (n = 24)	PS (n = 16)	PI (n = 13)	*P* Value
General	GA at evaluation (wk)	20.9 ± 2.4	19.9 ± 1.9	21.7 ± 3.4	NS
	Quintero Stage	0/24 (0)	3/16 (19)	0/13 (0)	.0006
	II	10/24 (42)	12/16 (75)	11/13 (85)	
	III	14/24 (58)	1/16 (6)	2/13 (15)	
	IV				
	CT ratio	0.45 ± 0.06*	0.41 ± 0.05	0.36 ± 0.06	.001
	DA retrograde flow	22/22 (100)	4/15 (27)	1/11 (9)	<.0001
	Hydrops	14/24 (58)	1/16 (6)	2/13 (15)	.0008
Function	≥Moderate RV dysfunction	22/23 (96)	4/16 (25)	8/13 (62)	<.0001
	≥Moderate TR	22/24 (92)	12/16 (75)	6/13 (46)	.009
	DV flow reversal	21/24 (88)	6/15 (40)	8/13 (62)	.008
	UV pulsation	10/24 (42)	3/15 (20)	2/13 (15)	NS
RV morphology	≥Moderate RV hypertrophy	17/22 (77)	9/16 (56)	6/13 (46)	NS
	RV hypoplasia	3/24 (13)	0/16 (0)	0/13 (0)	NS
	Z_{RVEDD}	0.7 ± 1.6	−0.4 ± 1.2	0.5 ± 1.2	NS
	Z_{TV}	−0.7 ± 1.3	−1.4 ± 1.4	−0.7 ± 1.3	NS
	Z_{PV}	−0.6 ± 1.3	−1.3 ± 1.5*	0.7 ± 0.8	.03
	Z_{MPA}	0.0 ± 0.9	1.5 ± 1.3†	0.4 ± 0.8	.009

Data are presented as mean ± standard deviation or frequency/total observations (%). For denominators <total number in each group, data were not available for all subjects. For intergroup comparisons (ANOVA with Bonferroni correction): *$P < .05$ vs. PI; †$P < .05$ vs. PA.
ANOVA, analysis of variance; CT, cardiothoracic; DA, ductus arteriosus; DV, ductus venosus; GA, gestational age; MPA, main pulmonary artery; NS, not statistically significant; PA, pulmonary atresia; PI, isolated pulmonary insufficiency; PS, pulmonary stenosis; PV, pulmonary valve annulus; RV, right ventricle; RVEDD, right ventricular end-diastolic dimension; TR, tricuspid regurgitation; TV, tricuspid valve annulus; UV, umbilical vein.

Michelfelder E, Tan X, Cnota J, Divanovic A, Statile C, Lim FY, Crombleholme T. Prevalence, Spectrum, and Outcome of Right Ventricular Outflow Tract Abnormalities in Twin-twin Transfusion Syndrome: A Large, Single-center Experience. Congenit Heart Dis. 2015 May-Jun;10(3):209-18.

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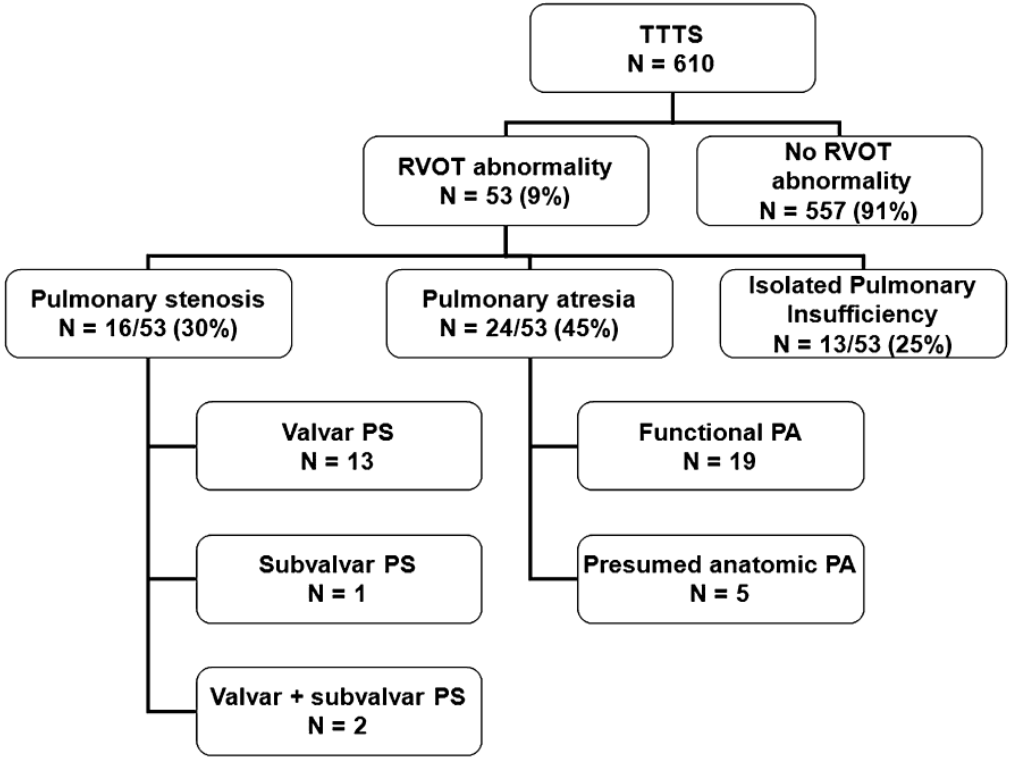

Figure 1. Study population with distribution of right ventricular outflow tract (RVOT) abnormalities by type. PA, pulmonary atresia; PS, pulmonary stenosis; TTTS, twin–twin transfusion syndrome.

Michelfelder E, Tan X, Cnota J, Divanovic A, Statile C, Lim FY, Crombleholme T. Prevalence, Spectrum, and Outcome of Right Ventricular Outflow Tract Abnormalities in Twin-twin Transfusion Syndrome: A Large, Single-center Experience. Congenit Heart Dis. 2015 May-Jun;10(3):209-18.

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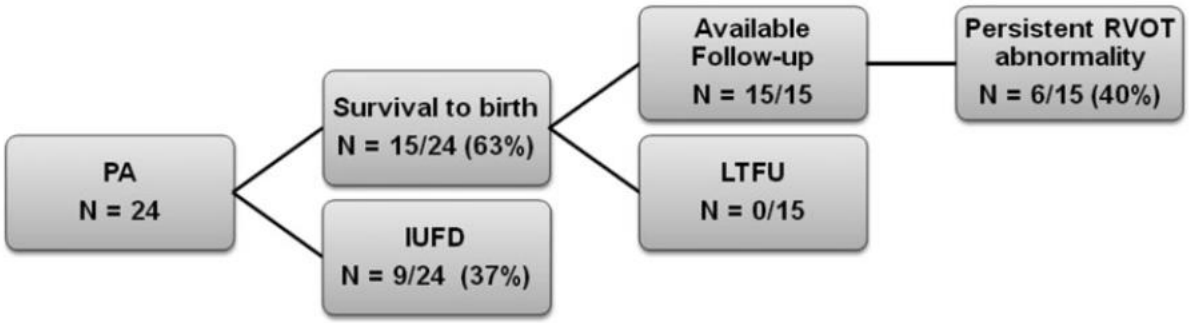

Figure 3. Postnatal cardiac outcomes in recipient twins with pulmonary atresia (PA). IUFD, intrauterine fetal demise; LTFU, lost to follow-up; RVOT, right ventricular outflow tract.

Michelfelder E, Tan X, Cnota J, Divanovic A, Statile C, Lim FY, Crombleholme T. Prevalence, Spectrum, and Outcome of Right Ventricular Outflow Tract Abnormalities in Twin-twin Transfusion Syndrome: A Large, Single-center Experience. Congenit Heart Dis. 2015 May-Jun;10(3):209-18.

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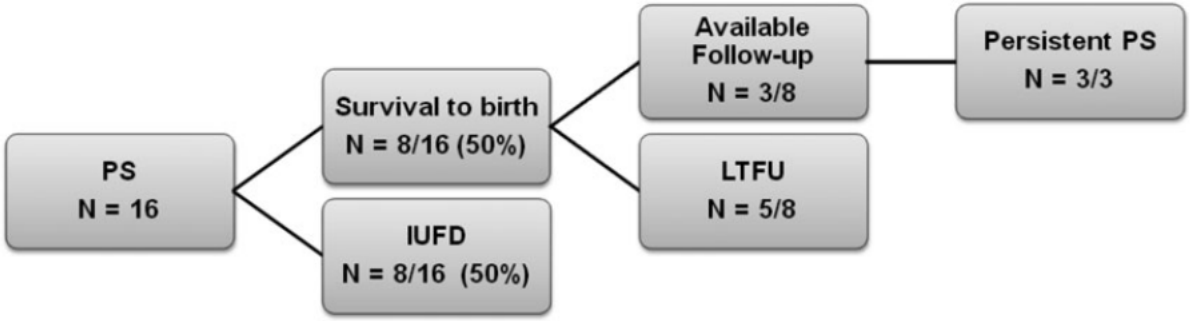

Figure 4. Postnatal cardiac outcomes in recipient twins with pulmonary stenosis (PS). IUFD, intrauterine fetal demise; LTFU, lost to follow-up.

Michelfelder E, Tan X, Cnota J, Divanovic A, Statile C, Lim FY, Crombleholme T. Prevalence, Spectrum, and Outcome of Right Ventricular Outflow Tract Abnormalities in Twin-twin Transfusion Syndrome: A Large, Single-center Experience. Congenit Heart Dis. 2015 May-Jun;10(3):209-18.

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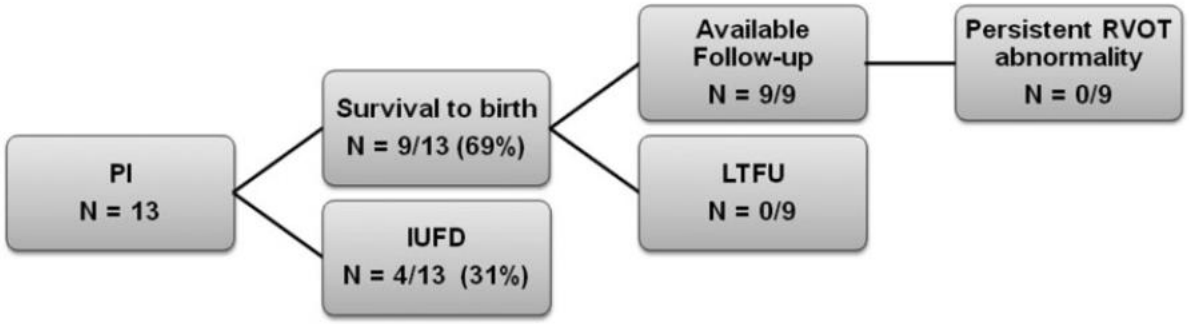

Figure 5. Postnatal cardiac outcomes in recipient twins with isolated pulmonary insufficiency (PI). IUFD, intrauterine fetal demise; LTFU, lost to follow-up; RVOT, right ventricular outflow tract.

Michelfelder E, Tan X, Cnota J, Divanovic A, Statile C, Lim FY, Crombleholme T. Prevalence, Spectrum, and Outcome of Right Ventricular Outflow Tract Abnormalities in Twin-twin Transfusion Syndrome: A Large, Single-center Experience. Congenit Heart Dis. 2015 May-Jun;10(3):209-18.

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Right ventricular outflow tract obstruction (RVOTO)

Table 2 Pulmonary valve findings prior to selective fetoscopic laser photocoagulation (SFLP) and at follow-up (postnatal or autopsy)

Case	*Prenatal echo findings*	*GA at SFLP (weeks)*	*GA at delivery (weeks)*	*BW (g)*	*Postnatal findings (echo/autopsy)*	*Postnatal course*
2	PI, dysplasia without turbulence by color Doppler, ductal flow reversal	23 + 5	IUFD	—	Normal PV at autopsy	
3	PI, dysplasia with turbulence, 1.9 m/s peak systolic gradient	23 + 3	28 + 2	870	Valvar pulmonary stenosis	Balloon pulmonary valvuloplasty at 10 weeks
4	PI developed after SFLP (reversal of TTTS), no turbulence	18 + 5	TOP 23 + 4	—	Normal PV at autopsy	
7	Normal initially, PI developed prior to SFLP, no turbulence or systolic gradient	22 + 4	34	2060	Normal	
10	PI, dysplasia, ductal flow reversal, no turbulence or systolic gradient	19 + 6	38 + 3	3060	Valvar pulmonary stenosis	Balloon pulmonary valvuloplasty at 3 months
11	PI only, no turbulence or systolic gradient	20 + 4	38	2640	Normal	
14	PI, no turbulence or systolic gradient	21 + 1	26	878	ASD, PDA	No cardiac intervention
16	PI, dysplasia, no turbulence or systolic gradient, intermittent ductal flow reversal	24	29 + 2	1737	Normal	RV function and TR improved after birth, normal at 1 month

ASD, atrial septal defect; BW, birth weight; GA, gestational age; IUFD, intrauterine fetal death; PDA, patent ductus arteriosus; PI, pulmonary insufficiency; PV, pulmonary valve; RV, right ventricle; TOP, termination of pregnancy; TR, tricuspid regurgitation; TTTS, twin–twin transfusion syndrome.

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Effect of selective fetoscopic laser photocoagulation therapy for twin–twin transfusion syndrome on pulmonary valve pathology in recipient twins

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Moon-Grady AJ, Rand L, Lemley B, Gosnell K, Hornberger LK, Lee H. Effect of selective fetoscopic laser photocoagulation therapy for twin-twin transfusion syndrome on pulmonary valve pathology in recipient twins. Ultrasound Obstet Gynecol. 2011 Jan;37(1):27-33.

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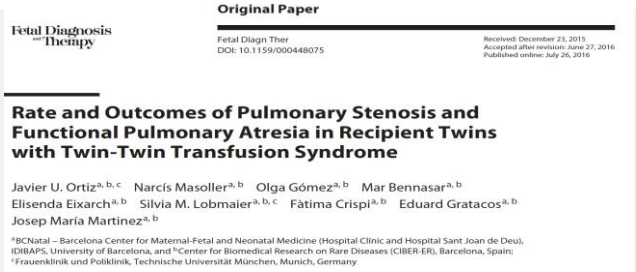

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Rate and Outcomes of Pulmonary Stenosis and Functional Pulmonary Atresia in Recipient Twins with Twin-Twin Transfusion Syndrome

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Table 1. Baseline characteristics and outcomes in the study groups

	No PS/PA (n = 232)	PS/PA (n = 28)	p value
Maternal age, years	32.5 (29–35)	32.5 (28.3–35.9)	0.891[a]
Quintero stages III–IV	101 (43.5%)	25 (89.3%)	<0.001
DV RF	44 (19.0%)	14 (50.0%)	<0.001
TR	38 (16.4%)	17 (60.7%)	<0.001
GA at surgery, weeks	19.6 (17.4–21.8)	19.5 (17.1–23.5)	0.713[a]
Miscarriage	22 (9.5%)	3 (10.7%)	0.742[b]
Preterm premature rupture of membranes <32 weeks[c]	49 (21.1%)	8 (28.6%)	0.370
Preterm delivery <32 weeks[c]	79 (34.1%)	13 (46.4%)	0.253
GA at delivery, weeks[c]	34.2 (31.0–36.6)	32.1 (27.5–36.0)	0.074
Survival of at least one twin at 6 months of age	194 (83.6%)	19 (67.9%)	0.045
Overall survival at 6 months of age	338/464 (72.8%)	32/56 (57.1%)	0.015

Data are given as median (interquartile range) or n (%).
[a] Mann-Whitney U test. [b] Fisher's exact test. [c] Excluded miscarriage.

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Table 2. Ultrasound findings, pregnancy outcomes and postnatal cardiologic follow-up data of surviving recipient twins with PS/PA prior to fetal surgery

Case No.	Prenatal diagnosis	TTTS stage	GA at diagnosis, weeks	GA at delivery, weeks	Type of birth	Birth weight, g	Postnatal diagnosis	Postnatal intervention	Echocardiography at 6 months
1	PA	III	22.4	36.0	vaginal	2,500	normal	no	–
2	PA	III	27.2	34.2	CS	2,140	normal	no	–
5	PS	I	21.0	34.6	vaginal	2,190	severe PS	valvotomy at 15 days after PBPV failure at 6 days	severe PS
8	PS	III	21.2	33.0	CS	1,860	PA, hypoplastic RV	univentricular staged surgery at 15 days	exitus after surgery
9	PS	III	19.0	33.0	CS	2,040	normal	no	–
10	PA	IV	23.3	36.2	CS	2,340	normal	no	–
11	PS	III	19.2	32.5	CS	2,160	severe PS	PBPV at 10 days and 6 months	severe PS
13	PS	II	20.0	30.0	CS	1,380	severe PS	PBPV at 24 days	mild PS
14	PS	III	17.5	39.4	vaginal	3,000	severe PS	PBPV at 7 days	normal
16	PS	III	16.4	31.3	CS	1,930	normal	no	–
17	PA	III	24.5	32.0	CS	1,630	normal	no	–
20	PS	I	19.6	31.4	vaginal	1,790	severe PS	PBPV at 16 days	normal
21	PS	III	17.1	34.5	vaginal	1,950	severe PS	PBPV at 20 days	mild PS
22	PS	III	32.2	35.2	CS	2,250	normal	no	–
23	PA	III	15.5	32.4	CS	1,900	normal	no	–
25	PS	III	17.2	30.5	CS	1,600	severe PS	PBPV at 21 days	normal
27	PS	III	25.5	34.4	vaginal	2,300	severe PS	PBPV at 10 days	normal
28	PA	III	26.6	36.2	CS	2,330	normal	no	–

CS = Cesarean section; RV = right ventricle.

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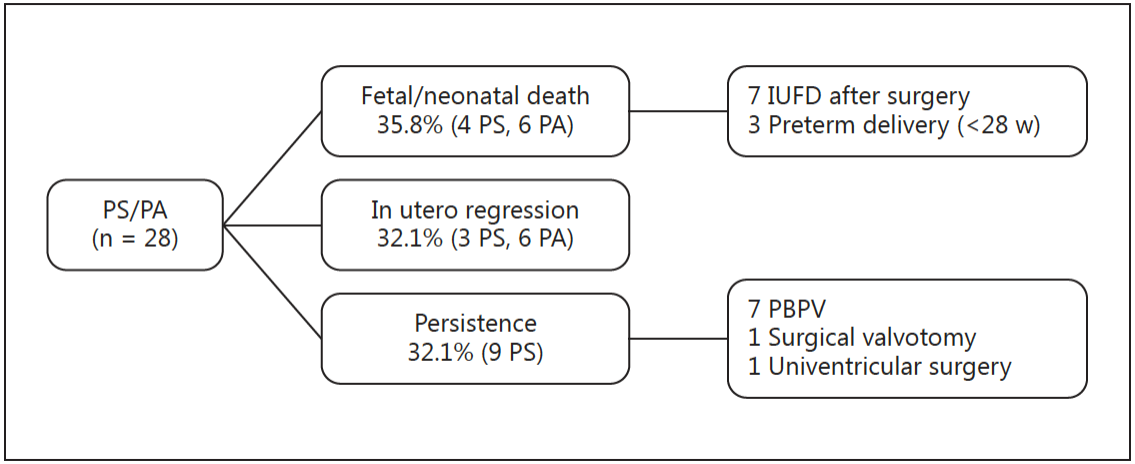

Fig. 2. Follow-up of recipient twins with PS/PA after laser surgery. IUFD = Intrauterine fetal death.

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Table 1 Ultrasound findings at time of fetal intervention in 14 complicated monochorionic twin pregnancies with a postnatal diagnosis of right ventricular outflow tract obstruction (RVOTO)

Case	*Diagnosis*	*Twin with RVOTO*	*Intervention*	*GA at intervention (weeks)*	*Intertwin EFW discordance (%)*	*DV flow in A-wave*	*Cardiomegaly*	*Tricuspid insufficiency*	*Pericardial effusion*
1	TTTS QS-II	Recipient	FLC	15 + 6	22.1	Positive	No	No	No
2a	TTTS QS-III	Donor	FLC	19 + 6	30.5	NK	NK	NK	NK
2b	TTTS QS-III	Recipient	FLC	19 + 6	30.5	Reversed	Yes	No	Yes
3	TTTS QS-III	Recipient	FLC	16 + 0	37.7	Absent	No	No	No
4	TTTS QS-III	Recipient	FLC	20 + 0	33.4	Reversed	No	No	Yes
5	TTTS QS-III	Recipient	FLC	17 + 2	26.3	Positive	No	No	No
6	TTTS QS-III	Recipient	FLC	14 + 3	4.0	Positive	No	No	No
7	TTTS QS-IV	Recipient	FLC	22 + 3	6.1	Reversed	No	No	Yes
8	TTTS QS-III	Recipient	FLC	19 + 5	29.3	Reversed	Yes	No	No
9	TTTS QS-III	Recipient	FLC	14 + 4	23.5	Reversed	Yes	NK	Yes
10	TTTS QS-III	Recipient	FLC	16 + 1	32.1	Reversed	No	Yes	No
11	TTTS QS-IV	Recipient	FLC	15 + 5	5.8	Reversed	Yes	Yes	Yes
12	sIUGR	Larger	None	—	—	—	—	—	—
13	sIUGR*	Larger	UCC	18 + 5	45.6	Positive	Yes	NK	Yes
14	sIUGR†	Larger	UCC	18 + 0	36.8	Positive	No	NK	Yes

*sIUGR twin with abnormal cerebellum and hydrocephalus. †sIUGR twin with omphalocele and hydrocephalus. DV, ductus venosus; EFW, estimated fetal weight; FLC, fetoscopic laser coagulation of anastomoses; GA, gestational age; NK, not known (missing data); QS, Quintero Stage; sIUGR, selective intrauterine growth restriction; TTTS, twin-to-twin transfusion syndrome; UCC, selective feticide by umbilical cord coagulation.

Eschbach SJ, Boons LSTM, Van Zwet E, Middeldorp JM, Klumper FJCM, Lopriore E, Teunissen AKK, Rijlaarsdam ME, Oepkes D, Ten Harkel ADJ, Haak MC. Right ventricular outflow tract obstruction in complicated monochorionic twin pregnancy. Ultrasound Obstet Gynecol. 2017 Jun;49(6):737-743.

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Table 2 Details of diagnosis and treatment of monochorionic twin pregnancies with postnatal diagnosis of right ventricular outflow tract obstruction (RVOTO)

Case	*GA at delivery (weeks)*	*Birth weight (g)*	*Prenatal diagnosis of RVOTO*	*Postnatal diagnosis of RVOTO*	*Intervention*	*Age at intervention (weeks)*	*Follow-up*
1	29 + 3	1135	Yes	Severe valvular PS	Balloon valvuloplasty	4	A&W
2a	26 + 3	720	Yes	Valvular PS	Balloon valvuloplasty	42	A&W
2b	26 + 3	865	Yes	Severe valvular PS, hypoplastic RV	None*		NND at 1 week
3	27 + 0	955	No	Severe valvular PS	Balloon valvuloplasty	18	A&W
4	38 + 3	3420	Yes	Severe valvular PS, hypoplastic RV	Balloon valvuloplasty, second balloon valvuloplasty†	< 1 < 1	Tay-Sachs disease
5	31 + 0	1400	Yes	Severe valvular PS, small RV	Rashkind procedure, balloon valvuloplasty	4	A&W
6	26 + 5	960	Yes	Mild PS	None		A&W
7	36 + 5	2250	Yes	Mild PS	None		A&W
8	32 + 2	1845	Yes	Severe PS, mild Ebstein's anomaly	Balloon valvuloplasty	19	A&W
9	39 + 0	3260	Yes	Severe PS, mild Ebstein's anomaly	Balloon valvuloplasty	< 1	A&W
10	29 + 0	1205	Yes	Pulmonary atresia	Balloon valvuloplasty	3	A&W
11	34 + 3	2160	Yes	Severe PS, massive TI	None‡		NND at 5 days
12	34 + 4	2630	Yes	Severe PS, RV hypertrophy	Balloon valvuloplasty	< 1	A&W
13	37 + 3	2565	Yes	Severe PS, RV hypertrophy	Balloon valvuloplasty, BT shunt, 1.5-ventricle repair§	< 1 6 2.5 years	A&W
14	37 + 6	3155	Yes	Severe valvular PS, dysplastic bicuspid valve	Balloon valvuloplasty	10	A&W

Pulmonary stenosis (PS): mild, peak gradient 2–3 m/s; moderate, 3–4 m/s; severe, > 4 m/s). *Neonatal death (NND) due to prematurity, cardiac failure with cerebral abnormalities and infant respiratory distress syndrome. †Successful balloon valvuloplasty on day 1 with redilatation after 10 weeks because of increasing PS. ‡NND due to cardiac failure combined with *Escherichia coli* sepsis. §Glenn procedure (bidirectional cavopulmonary shunt). A&W, alive and well; BT shunt, Blalock–Taussig shunt; GA, gestational age; RV, right ventricle; TI, tricuspid insufficiency.

Eschbach SJ, Boons LSTM, Van Zwet E, Middeldorp JM, Klumper FJCM, Lopriore E, Teunissen AKK, Rijlaarsdam ME, Oepkes D, Ten Harkel ADJ, Haak MC. Right ventricular outflow tract obstruction in complicated monochorionic twin pregnancy. Ultrasound Obstet Gynecol. 2017 Jun;49(6):737-743.

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Table 4 Predicted risk for right ventricular outflow tract obstruction at birth in recipient twins of twin-to-twin transfusion syndrome (TTTS) according to gestational age (GA) at diagnosis, presence of pericardial effusion (PE) and flow in ductus venosus (DV)

GA at diagnosis of TTTS (weeks)	*PE absent*		*PE present*	
	Normal DV	*Abnormal DV*	*Normal DV*	*Abnormal DV*
15	4	20	43	82
16	3	16	35	77
17	2	12	28	70
18	2	9	22	63
19	1	6	17	55
20	1	5	13	47
21	1	3	10	39
22	0	3	7	31
23	0	2	5	25
24	0	1	4	19
25	0	1	3	14
26	0	1	2	11

Data are given as percentage risk.

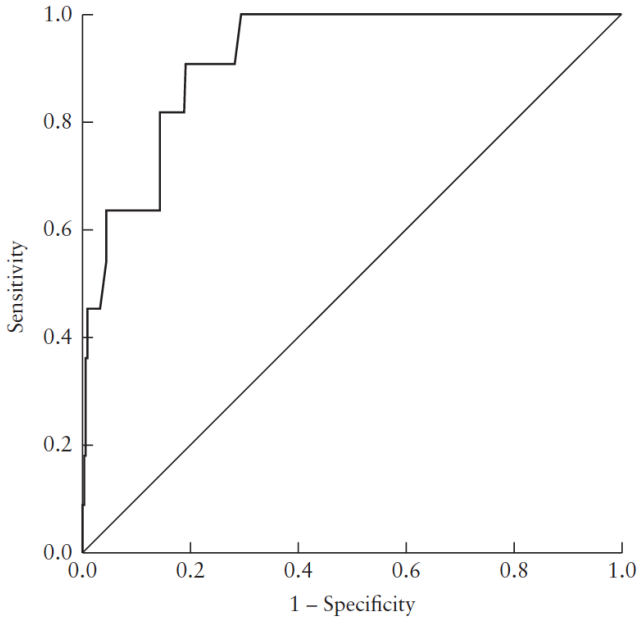

Figure 1 Receiver–operating characteristics (ROC) curve for prediction of right ventricular outflow tract obstruction at birth in recipient twin of twin-to-twin transfusion syndrome (TTTS) using model incorporating gestational age at diagnosis of TTTS and presence of pericardial effusion and abnormal flow in the ductus venosus. Area under ROC curve, 0.92.

Eschbach SJ, Boons LSTM, Van Zwet E, Middeldorp JM, Klumper FJCM, Lopriore E, Teunissen AKK, Rijlaarsdam ME, Oepkes D, Ten Harkel ADJ, Haak MC. Right ventricular outflow tract obstruction in complicated monochorionic twin pregnancy. Ultrasound Obstet Gynecol. 2017 Jun;49(6):737-743.

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Improved recipient survival with maternal nifedipine in twin-twin transfusion syndrome complicated by TTTS cardiomyopathy undergoing selective fetoscopic laser photocoagulation

Timothy M. Crombleholme, MD; Foong-Yen Lim, MD; Mounira Habli, MD; William Polzin, MD; Ronald Jaekle, MD; Erik Michelfelder, MD; James Cnota, MD; Chunyan Liu, MS; Mi-Ok Kim, PhD

Crombleholme TM, Lim FY, Habli M, Polzin W, Jaekle R, Michelfelder E, Cnota J, Liu C, Kim MO. Improved recipient survival with maternal nifedipine in twin-twin transfusion syndrome complicated by TTTS cardiomyopathy undergoing selective fetoscopic laser photocoagulation. Am J Obstet Gynecol. 2010 Oct;203(4):397.e1-9.

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TABLE 1
Cincinnati staging system and classifications of recipient cardiomyopathy

Stage	Donor	Recipient	Recipient cardiomyopathy
Cincinnati staging system			
I	Oligohydramnios (DVP <2 cm)	Polyhydramnios (DVP >8 cm)	No
II	Absent bladder	Bladder seen	No
III	Abnormal Doppler findings	Abnormal Doppler findings	None
IIIa			Mild
IIIb			Moderate
IIIc			Severe
IV	Hydrops	Hydrops	
V	Death	Death	
Classifications of recipient cardiomyopathy			
Variables/cardiomyopathy	Mild	Moderate	Severe
Atrioventricular valve regurgitation	Mild	Moderate	Severe
Right/left ventricular hypertrophy	Mild	Moderate	Severe
Myocardial performance index[a]	>+2 Z-score	>+3 Z-score	>+4 Z-score or severe biventricular dysfunction
Left	>0.43	>0.48	>0.53
Right	>0.48	>0.56	>0.64

DVP, deepest vertical pocket.

[a] Standards at our institution (mean ± SD): left = 0.33 ± 0.05; right = 0.32 ± 0.08.

Crombleholme. Maternal nifedipine improves recipient survival in TTTS. Am J Obstet Gynecol 2010.

Crombleholme TM, Lim FY, Habli M, Polzin W, Jaekle R, Michelfelder E, Cnota J, Liu C, Kim MO. Improved recipient survival with maternal nifedipine in twin-twin transfusion syndrome complicated by TTTS cardiomyopathy undergoing selective fetoscopic laser photocoagulation. Am J Obstet Gynecol. 2010 Oct;203(4):397.e1-9.

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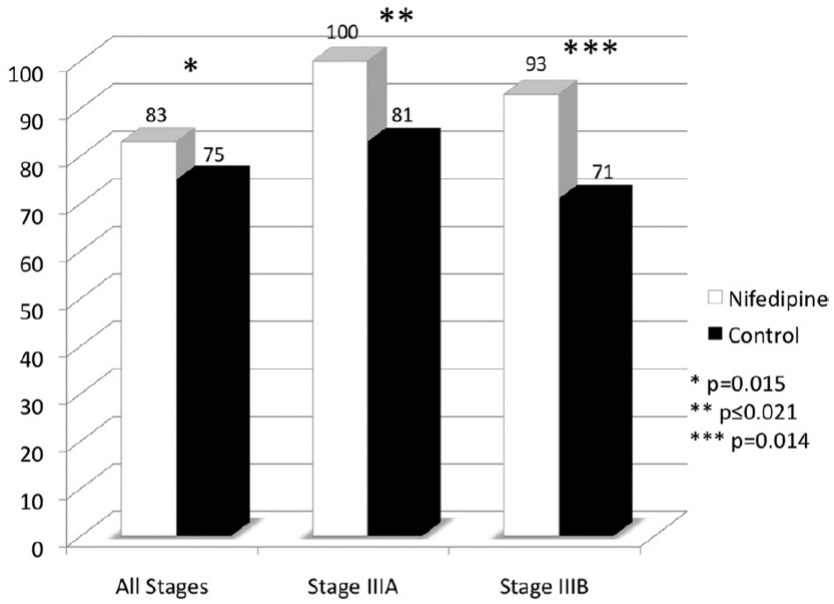
FIGURE 1
Effect on survival of maternal nifedipine



The *y axis* is the percent survival to birth. On the *x axis* are the treatment groups. *All* represents the entire cohort; *stage IIIA* and *IIIB* represent the recipient outcomes by stage. The *open columns* represent the nifedipine-treated group; the *closed columns* represent the gestational age- and stage-matched control subjects. Because there was no statistically significant difference in survival for stages IIIC and IV, they are not depicted. The *single asterisk* indicates a probability value of .017; the *double asterisk* indicates a probability value of ≤ .021; the *triple asterisk* indicates a probability value of .014.

Crombleholme. Maternal nifedipine improves recipient survival in TTTS. Am J Obstet Gynecol 2010.

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TABLE 5

Summary of Cardiovascular Considerations for Twins Surviving TTTS

For 'ex-recipient'	For 'ex-donor'
Resolving cardiomyopathy	
Right ventricular outflow tract obstruction –unpredictable response to treatment	Coarctation of the aorta – difficult to exclude antenatally
Blood pressure	Blood pressure
Persistent pulmonary hypertension of the newborn	Cardiac consequences of severe IUGR

Manning N, Archer N. Cardiac Manifestations of Twin-to-Twin Transfusion Syndrome. Twin Res Hum Genet. 2016 Jun;19(3):246-54.

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