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Does transatrial-transpulmonary approach improve outcomes compared with transventricular approach in non-neonatal patients undergoing tetralogy of Fallot repair?

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Summary

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was whether the transatrial-transpulmonary approach to tetralogy of Fallot repair in non-neonatal patients provides superior outcomes compared with the transventricular approach. Altogether, 175 papers were found using the reported search, of which 11 represented the best evidence to answer the clinical question. Two randomized controlled trials (RCTs) and 3 observational studies showed that the transatrial approach resulted in better preservation of right ventricular (RV) function, whereas 4 observational studies showed no significant difference. Three observational studies showed better attenuation of RV dilatation, whereas 3 showed no difference. One RCT and 2 observational studies showed no difference. Two observational studies demonstrated greater freedom from reoperation, 1 RCT and 4 observational studies showed no difference, while 1 retrospective study observed a higher incidence of residual RV outflow tract obstruction and lower freedom from reoperation in infants. Two observational studies reported lower risk of requiring pulmonary valve replacement, whereas 2 reported no difference. Three observational studies reported superior exercise capacity, while 1 reported no difference. No difference in long-term survival was demonstrated. The results presented suggest that transatrial repair of tetralogy of Fallot confers superior or equivalent outcomes in terms of preservation of RV function and volume, ventricular arrhythmias, need for pulmonary valve replacement, and exercise capacity compared with transventricular repair. However, the incidence of residual RV outflow tract obstruction may be higher in infants undergoing transatrial repair.

Keywords: Tetralogy of Fallot • Transatrial • Transventricular • Evidence-based medicine • Review

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This protocol is fully described in the *ICVTS* [1].

THREE-PART QUESTION

In [non-neonatal patients undergoing repair of tetralogy of Fallot (TOF)], does [transatrial-transpulmonary approach or transventricular approach] provide superior [outcomes]?

CLINICAL SCENARIO

A 2-week-old acyanotic infant was diagnosed at birth with TOF. Surgical repair is scheduled for when the baby is 5 months old. You plan to perform the repair via the transventricular approach, but your colleague suggests that outcomes are not as good as the transatrial approach. You search the literature to look for evidence.

SEARCH STRATEGY

MEDLINE was searched from 1950 to January 2019 using the PubMed interface: ((tetralogy OR Fallot) AND repair) AND (transatrial OR transpulmonary OR transventricular OR ventriculotomy).

SEARCH OUTCOME

A total of 175 papers were found using the reported search, of which 11 were selected as providing the best evidence on this topic (Table 1).

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Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Kawashima <i>et al.</i> (1985), J Thorac Cardiovasc Surg, Japan [5] Retrospective cohort (level III)	n = 90: transpulmonary (group 1) n = 21: transventricular (group 2)	Late mortality	Nil	Limitation: non-concurren periods
		PR (grade ≥2/4)	47% vs 81% (P < 0.05)	
		RV EDVi during isoproterenol in- fusion (ml/m ²)	81 ± 21 vs 109 ± 30 (P < 0.01)	
	Mean age: 6.9 vs 8.9 years	RV EF during isoproterenol infu- sion	57% ± 4% vs 49% ± 6% (<i>P</i> < 0.001)	
		Ventricular arrhythmia (Lown grade ≥2)	17% vs 54% (P < 0.001)	
Miura <i>et al.</i> (1992), J Thorac Cardiovasc Surg, Japan [<mark>6</mark>]	n = 17: transatrial-transpul- monary, without ventriculot- omy (group la) n = 22: transatrial-transpul- monary, minimal RV-otomy (group lb) n = 23: transventricular (group II) Mean age: 6.6 years Mean follow-up: 3.7 years	RV anterior wall motion at rest (fractional area change, %):		Limitations: non-concur- rent periods; different myocardial protection
		Upper parts	la: 32 ± 11	inyocardia protection
Retrospective cohort (level III)			lb: 21 ± 8 (P < 0.001 vs la)	
			II: 18 ± 7 (<i>P</i> < 0.001 vs la; <i>P</i> = NS vs Ib)	
		Middle parts	la: 38 ± 5	
			lb: 35 ± 7 (P = NS vs Ia)	
			II: 25 ± 6 (<i>P</i> < 0.001 vs la; <i>P</i> < 0.001 vs lb)	
		Lower parts	la: 37 ± 7	
			lb: 32 ± 7 (P < 0.05 vs la)	
			II: 25 ± 6 (<i>P</i> < 0.001 vs la; <i>P</i> < 0.005 vs lb)	
		RVEF (%):		
		At rest	la: 58 ± 8	
			lb: 56 ± 7 (<i>P</i> = NS vs la)	
			II: 51 ± 5 (<i>P</i> < 0.001 vs la; <i>P</i> < 0.001 vs lb)	
		During isoproterenol infusion (P: compared to at rest)	la: 65 ± 6 (P < 0.05)	
			Ib: 61 ± 6 (<i>P</i> < 0.001)	
			II: 53 ± 5 (<i>P</i> = NS)	
Dietl <i>et al.</i> (1994), Circulation Argentina [7]	n = 71: transventricular	Atrial flutter	4.2% vs 0%	Limitations: retrospective;
Circulation, Argentina [7] Retrospective cohort (level III)	(group A) n = 36: transatrial (group B)	Ventricular arrhythmias (Lown grade ≥2)	39.4% vs 2.8% (P < 0.001)	non-concurrent periods
	Mean age: 6.8 vs 7.9 years	Late deaths	5.6% vs 2.8%	
	Mean follow-up: 9.7 vs 7.2 years	Satisfactory RV function	66.7% vs 83.3% (P < 0.01)	
		Moderate-to-severe PR	25.9% vs 12.5% (P < 0.01)	
Stellin <i>et al.</i> (1995), Ann Thorac Surg, Italy [8]	n = 22: transventricular (group A)	Early deaths	4.5% vs 0%	Limitations: non-concur- rent periods; limited fol- low-up of transatrial group
		Low output syndrome	18.2% vs 3.4%	

Continued

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(level iii)monary (group i) Maxa get 42 monthsFNOTO0% v3.4%Hereice is 162% v3.4%Mean get 42 monthsPulmonary stenois18.2% v3.4%	and country Study type	Patient group	Outcomes	Key results	Comments
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Retrospective cohort (level III) n = 69: transatrial (group 2) RVOT gradient >40 mmHg 6% vs 18% (P = 0.03) Limitations: patients were se- lected for transatrial repair if transannular patch was predicted Mean age: 200.2 vs 188.6 days Moderate PR 48% vs 28% (P = 0.007) Limitations: patients were se- lected for transatrial repair if transannular patch was predicted Mean follow-up: 14.5 vs 6 years Good biventricular function 97% vs 99% (P = 0.05) Penos 24-hour Holter: Recurrent ventricular tachycar- dia 1.7% vs 0% Fenos Nover the operations: 10-year freedom from reinter- 92% ± 3% vs 65% ± 6% Fenos			Echocardiography:		
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Moderate RV dilatation 32% vs 18% (P = 0.05) predicted Mean follow-up: 14.5 vs 6 Good biventricular function 97% vs 99% (P = NS) 24-hour Holter: 24-hour Holter: Recurrent ventricular tachycar- dia 1.7% vs 0% Reoperations: 10-year freedom from reinter- 92% ± 3% vs 65% ± 6% 92% ± 3% vs 65% ± 6%		days	Moderate PR	48% vs 28% (<i>P</i> = 0.007)	lected for transatrial repair if transannular patch was
yearsGood biventricular function97% vs 99% (P = NS)24-hour Holter:Recurrent ventricular tachycar- dia1.7% vs 0%Reoperations:10-year freedom from reinter-92% ± 3% vs 65% ± 6%			Moderate RV dilatation	32% vs 18% (P=0.05)	
Recurrent ventricular tachycar- dia Reoperations: 10-year freedom from reinter- 92% ± 3% vs 65% ± 6%		•	Good biventricular function	97% vs 99% (P = NS)	
dia Reoperations: 10-year freedom from reinter- 92% ± 3% vs 65% ± 6%			24-hour Holter:		
10-year freedom from reinter- 92% ± 3% vs 65% ± 6%				1.7% vs 0%	
			Reoperations:		

Table 1: Continued				
Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
		10-year freedom from RVOTO reoperation	98% ± 2% vs 73% ± 6% (<i>P</i> < 0.0001)	
		10-year freedom from PVR	97% ± 2% vs 100% (<i>P</i> = NS)	
Sun <i>et al.</i> (2013), Asian J Surg, China [11] Prospective randomized controlled trial (level II)	n = 53: transatrial-transpul- monary (group A) n = 53: transventricular (group B) Mean age: 11.53 vs 10.43	Perioperative outcomes:		Limitations: short follow- up; no CMR data available on RV function
		Cardiopulmonary bypass (min)	95.02 ± 23.8 vs 85.23 ± 22.63 (<i>P</i> = 0.032)	
		Cross-clamp (min)	69.4 ± 10.36 vs 61.17 ± 9.38 (<i>P</i> = 0.035)	
	months ($P = NS$)	Inotropic support (days)	1.63 ± 0.97 vs 2.1 ± 1.09 (P = 0.02)	
	Mean follow-up: 39.6 months	Intubation (h)	26.62 ± 12.48 vs 33.02 ± 17.55 (<i>P</i> = 0.033)	
		Intensive care (days)	2.25 ± 1.28 vs 2.85 ± 1.46 (<i>P</i> = 0.026)	
		Perioperative complications:		
		Reoperation	5.7% vs 0% (P = 0.079)	
		Low cardiac output	1.9% vs 9.4% (<i>P</i> = 0.093)	
		Arrhythmias	5.7% vs 18.9% (<i>P</i> = 0.038)	
		Follow-up:		
		Arrhythmias	1.89% vs 14% (<i>P</i> = 0.024)	
		RVOT gradient (mmHg)	12.16 ± 5.56 vs 11.6 ± 6.84 (<i>P</i> = NS)	
		Moderate-to-severe PR	5.66% vs 20% (<i>P</i> = 0.056)	
		Mild-moderate RV dysfunction	0% vs 8% (<i>P</i> = 0.036)	
Lee et al. (2014),	n = 39: limited RV-otomy (transatrial) (group 1) n = 74: conventional RV- otomy (group 2) Mean age: 1.8 vs 3.3 years (P = 0.007) Mean interval between re- pair and CMR: 12.7 vs 17.2 years (P < 0.001)	RV EDVi (ml/m ²)	149 ± 31 vs 152 ± 48 (P = NS)	No long-term benefits of limited RV-otomy in terms of RV volume and function, but transatrial-transpulmonary approach was not discour- aged Limitations: only included patients who had CMR; vari- able surgical techniques
J Thorac Cardiovasc Surg, South Korea [2] Retrospective cohort (level III)		RV EF	54% ± 9% vs 52% ± 10% (<i>P</i> = NS)	
		Freedom from PVR at 20 years	29.5% ± 14.5% vs 38.1% ± 6.1% (<i>P</i> = NS)	
		Reoperation for RVOTO	0% vs 2.7% (<i>P</i> = NS)	
		Mortality	2.6% vs 0% (P = NS)	
		Arrhythmia	0% vs 2.7% (<i>P</i> = NS)	
	Mean follow-up: 14.5 vs 21.1 years (<i>P</i> < 0.001)	Peak oxygen consumption (ml/ kg/min)	29 ± 6 vs 30 ± 6 (P = NS)	
	Propensity score-matched pairs			
Padalino <i>et al</i> . (2017), J Card Surg, Italy [<mark>12</mark>]	n = 42: transventricular (group 1)	Any adverse event	42.9% vs 32.4% (P = NS)	Limitations: inter-centre variability; different age
Retrospective cohort (level III)	n = 37: transatrial (group 2)	Reoperation	31.0% vs 16.2% (P = NS)	and associated procedures; only 26.8% of all patients

Continued

Author, date, journal	Patient group	Outcomes	Key results	Comments
and country Study type (level of evidence)				
	Median age: 1.0 vs 0.3 years (P < 0.001)	Peak oxygen uptake (ml/min/m ² , mean)	31.4 vs 39.5 (<i>P</i> = 0.006)	
	Median follow-up: 17.8 vs 15.7 years (P = NS)	11 RV EDVi (ml/m ²) rs 50 RV EF	130.15 vs 137.43 (<i>P</i> = NS)	
	CMR at median 10.5 years		50.96% vs 51.23% (<i>P</i> = NS)	
	after repair		31.24% vs 36.43% (P = NS)	
		Impact of transatrial repair, odds ratio (95% confidence interval):		
		PVR		
		Surgical reintervention	0.260 (0.071–0.954); <i>P</i> = 0.042	
Simon <i>et al.</i> (2019), Semin Thorac Cardiovasc Surg, USA [3] Retrospective cohort (level III)	n = 21: extended RV-otomy (group 1) n = 17: limited RV-otomy (group 2) Mean age: 3.8 vs 2.7 years (P = 0.001) Median follow-up: 30.9 years	Survival	30 years: 93.6% (<i>P</i> = NS)	Limitations: small sample; non-concurrent periods
		Freedom from reoperation	10 years: 57.1% vs 94.1% (P = 0.02)	
		Ventricular arrhythmias or sup- raventricular tachycardia Cumulative events (reoperation, arrhythmia or death)	25 years: 45% vs 55% (P = NS)	
			20 years: 7% vs 30% (P = NS)	
			30 years: 55% vs 35% (P = NS)	
			10 years: 42.9% vs 5.9% (P = 0.02) 20 years: 54.2% vs 21.8%	
			(P = 0.06)	
		Exercise endurance time (min, mean) Maximal oxygen consumption (% predicted, median)	25 years: 54% vs 50% (P = NS) 20 years: 9 vs 10 (P = NS)	
			30 years: 9 vs 12 (P = NS)	
			20 years: 75 vs 105 (P = 0.001)	
		RV end-diastolic diameter Z score	30 years: 70 vs 80 (P = NS)	
			20 years: 5.82 ± 1.93 vs 4.75 ± 2.30 (P = NS)	
			30 years: 5.55 ± 1.69 vs 4.14 ± 0.63 (P = 0.03)	

Data are presented as mean ± standard deviation or median (interquartile range).

CMR: cardiac magnetic resonance; EDVi: end-diastolic volume index; EF: ejection fraction; LV: left ventricle; NS: non-significant; PR: pulmonary regurgitation; PVR: pulmonary valve replacement; RV: right ventricle; RV-otomy: right ventriculotomy; RVEF: right ventricular ejection fraction; RVOTO: right ventricular outflow tract obstruction.

We could not find consensus in the literature on the extent of right ventricular (RV) infundibular incisions that defined transatrial versus transventricular repair. For example, Lee *et al.* [2] defined transatrial repair as involving 'limited' ventriculotomy <1 cm, whereas Simon *et al.* [3] used a cut-off of <2 cm. In comparison, Alexiou *et al.* [4] limited their infundibulotomy to 2–3 mm in transatrial repair and ventriculotomy to 1.5 cm in transventricular repair. Therefore, we defined the transatrial and transventricular approaches based on whether repair was mainly performed via the right atrium or the RV, respectively, regardless of the actual length of ventriculotomy.

RESULTS

Eleven clinical studies, including 2 prospective randomized controlled trials and 9 observational studies, reported the postoperative outcomes of patients who underwent TOF repair via the transventricular approach versus the transatrial-transpulmonary approach.

Kawashima *et al.* [5] demonstrated that transpulmonary TOF repair with or without minimal right ventriculotomy (RV-otomy) in 90 children resulted in smaller RV volume, greater RV ejection fraction and lower incidence of ventricular arrhythmia and pulmonary regurgitation (PR) compared with transventricular repair. There was no late mortality in either group.

Miura *et al.* [6] evaluated postoperative RV function by regional anterior wall motion analysis and RV ejection fraction in 62 patients. The 2 transatrial-transpulmonary groups, with and without minimal ventriculotomy respectively, had comparable regional wall motion and global RV function, while the transventricular group displayed impaired RV function at rest and minimal functional reserve under stress. The authors concluded that transatrial-transpulmonary repair provided better postoperative RV function and reserve than transventricular repair.

Similar findings were reported by Dietl *et al.* [7], who studied 107 patients and found that the transatrial approach was associated with a lower prevalence of RV dysfunction and moderate-to-severe PR at a mean follow-up of 8.9 years. Furthermore, the transatrial group had lower risk of postoperative life-threatening ventricular arrhythmias without a higher incidence of supraven-tricular arrhythmias. Late mortality and functional status were both excellent in the transatrial group.

Stellin *et al.* [8] showed that transatrial-transpulmonary repair could be performed in 51 neonates and infants younger than 6 months with minimal operative risk, good early haemodynamic results and a low incidence of residual lesions, which were comparable with transventricular repair. Similar to previous studies, they demonstrated reduced RV volume and better RV function in the transatrial group, although this was not statistically significant.

Atallah-Yunes *et al.* [9] studied the late functional status of 42 patients at >10 years after TOF repair. They found a similar incidence of residual RV outflow tract stenosis and PR between the 2 groups. However, the transatrial group had significantly less RV dilation, better preserved RV function, less need for pulmonary valve replacement, and better exercise endurance.

In the first prospective randomized controlled trial on this topic, Kaushal *et al.* [10] randomized 40 children equally to transatrial-transpulmonary and transventricular techniques. At 6months follow-up, equivalent outcomes were obtained in mortality, functional status and incidence of arrhythmia. However, the transventricular group had a higher incidence of RV global hypokinesia, which was of uncertain clinical significance given the limited follow-up.

In a large series of 160 infants, Alexiou *et al.* [4] found that both techniques were associated with an acceptably low incidence of arrhythmia, good biventricular function and excellent survival at a mean follow-up of 10.8 years. In contrast to previous studies in older children, this study in infants demonstrated no significant impact of ventriculotomy on RV function and late arrhythmia. Furthermore, the transatrial group had a significantly higher incidence of residual or recurrent RV outflow tract obstruction at early and mid-term even when a transannular patch was used, resulting in lower freedom from reoperation at 10 years. The authors suggested that concerns of possible RV dysfunction and arrhythmia should not discourage the use of transventricular repair in infants.

In the largest randomized controlled trial to date on this topic, Sun *et al.* [11] allocated 106 infants equally to repair with each technique. The transatrial-transpulmonary approach resulted in longer bypass and cross-clamp times, but shorter durations of intubation, inotropic support and intensive care stay and lower incidence of perioperative arrhythmias. Furthermore, at a mean follow-up of 39.6 months, the transatrial group had a lower incidence of RV impairment. No difference in mortality, functional status or residual RV outflow tract stenosis was demonstrated.

Lee *et al.* [2] analysed the cardiac magnetic resonance findings of 39 propensity score-matched pairs of children at long-term follow-up. In contrast to previous studies, indexed RV volumes and biventricular functions were similar between the conventional RV-otomy and limited RV-otomy groups. There was also no difference in freedom from reoperation, mortality, arrhythmia and exercise capacity. Although no long-term benefit of limited RV-otomy was demonstrated, the authors cautioned that the study population did not represent the entire spectrum of TOF patients, and that transatrial-transpulmonary repair should not be discouraged.

Padalino *et al.* [12] evaluated the long-term outcomes of 79 infants with cardiac magnetic resonance at a median of 10.5 years after TOF repair. They found no difference in the freedom from reintervention, RV volumes, function and PR between the 2 groups. However, the transatrial approach was protective for both pulmonary valve replacement and surgical reintervention on multivariate analysis. The authors concluded that transatrial repair may reduce the incidence of long-term adverse events.

Finally, Simon *et al.* [3] performed serial follow-up of 38 children at the first, second and third decade after TOF repair. Limited ventriculotomy conferred fewer cumulative adverse events (reoperation, arrhythmia or death) at 10 years, greater exercise capacity at 20 years and attenuated RV dilatation at 30 years. However, no difference was found at other time points and in 30-year survival.

CLINICAL BOTTOM LINE

Transatrial repair of TOF confers superior or equivalent outcomes in terms of preservation of RV function and volume, ventricular arrhythmias, need for pulmonary valve replacement and exercise capacity compared with transventricular repair. No difference in long-term survival was demonstrated. However, the incidence of residual RV outflow tract obstruction may be higher in infants undergoing transatrial repair.

Conflict of interest: Yves d'Udekem is a consultant for MSD and Actelion. He is also a National Health and Medical Research Council Clinician Practitioner Fellow [1082186]. All other authors declared no conflict of interest.

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