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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 lower incidence of postoperative ventricular arrhythmias, while 1 RCT and 4 observational studies showed no difference. Two observational studies demonstrated greater freedom from reoperation, 1 RCT and 2 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 *JCVTS* [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).

**Table 1:** Best evidence papers

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)	<i>n</i> = 90: transpulmonary (group 1)	Late mortality	Nil	Limitation: non-concurrent periods
		PR (grade $\geq 2/4$ )	47% vs 81% ( $P < 0.05$ )	
	<i>n</i> = 21: transventricular (group 2)	RV EDVi during isoproterenol infusion (ml/m <sup>2</sup> )	81 $\pm$ 21 vs 109 $\pm$ 30 ( $P < 0.01$ )	
	Mean age: 6.9 vs 8.9 years	RV EF during isoproterenol infusion	57% $\pm$ 4% vs 49% $\pm$ 6% ( $P < 0.001$ )	
		Ventricular arrhythmia (Low grade $\geq 2$ )	17% vs 54% ( $P < 0.001$ )	
Miura <i>et al.</i> (1992), J Thorac Cardiovasc Surg, Japan [6]  Retrospective cohort (level III)	<i>n</i> = 17: transatrial-transpulmonary, without ventriculotomy (group Ia)	RV anterior wall motion at rest (fractional area change, %):		Limitations: non-concurrent periods; different myocardial protection
		Upper parts	Ia: 32 $\pm$ 11	
	<i>n</i> = 22: transatrial-transpulmonary, minimal RV-otomy (group Ib)		Ib: 21 $\pm$ 8 ( $P < 0.001$ vs Ia)	
			II: 18 $\pm$ 7 ( $P < 0.001$ vs Ia; $P = NS$ vs Ib)	
	<i>n</i> = 23: transventricular (group II)	Middle parts	Ia: 38 $\pm$ 5	
	Mean age: 6.6 years		Ib: 35 $\pm$ 7 ( $P = NS$ vs Ia)	
	Mean follow-up: 3.7 years		II: 25 $\pm$ 6 ( $P < 0.001$ vs Ia; $P < 0.001$ vs Ib)	
		Lower parts	Ia: 37 $\pm$ 7	
			Ib: 32 $\pm$ 7 ( $P < 0.05$ vs Ia)	
			II: 25 $\pm$ 6 ( $P < 0.001$ vs Ia; $P < 0.005$ vs Ib)	
		RVEF (%):		
		At rest	Ia: 58 $\pm$ 8	
		Ib: 56 $\pm$ 7 ( $P = NS$ vs Ia)		
		II: 51 $\pm$ 5 ( $P < 0.001$ vs Ia; $P < 0.001$ vs Ib)		
	During isoproterenol infusion ( $P$ : compared to at rest)	Ia: 65 $\pm$ 6 ( $P < 0.05$ )		
		Ib: 61 $\pm$ 6 ( $P < 0.001$ )		
		II: 53 $\pm$ 5 ( $P = NS$ )		
Dietl <i>et al.</i> (1994), Circulation, Argentina [7]  Retrospective cohort (level III)	<i>n</i> = 71: transventricular (group A)	Atrial flutter	4.2% vs 0%	Limitations: retrospective; non-concurrent periods
	<i>n</i> = 36: transatrial (group B)	Ventricular arrhythmias (Low grade $\geq 2$ )	39.4% vs 2.8% ( $P < 0.001$ )	
	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]	<i>n</i> = 22: transventricular (group A)	Early deaths	4.5% vs 0%	Limitations: non-concurrent periods; limited follow-up of transatrial group
		Low output syndrome	18.2% vs 3.4%	

Continued

Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments	
Retrospective cohort (level III)	<i>n</i> = 29: transatrial-transpulmonary (group B)	Residual lesions: RVOTO	0% vs 3.4%		
	Mean age: 4.2 months	Pulmonary stenosis	18.2% vs 3.4%		
	Mean follow-up: 7.3 vs 2.1 years	Echocardiography (mean): RV EDV (ml/m <sup>2</sup> )	60.4 vs 55.6 ( <i>P</i> = NS)		
		RV EF	35.4% vs 41.8% ( <i>P</i> = NS)		
Atallah-Yunes <i>et al.</i> (1996), Circulation, USA [9]  Retrospective cohort (level III)	<i>n</i> = 20: transatrial (group 1)	Residual RVOT gradients (mmHg)	20 ± 12 vs 26 ± 16 ( <i>P</i> = NS)	Transatrial approach resulted in less RV dilation and better preservation of RV function	
	<i>n</i> = 22: transventricular (group 2)	PR	56% vs 35% ( <i>P</i> = NS)		
	Mean age: 2.7 vs 3.9 years ( <i>P</i> < 0.01)	Measures of RV size: RV/LV ratio	0.66 ± 0.22 vs 0.81 ± 0.17 ( <i>P</i> = 0.02)		
		Cardiothoracic ratio	0.53 ± 0.04 vs 0.58 ± 0.06 ( <i>P</i> = 0.03)		
	Mean follow-up: 12.2 vs 13.4 years ( <i>P</i> = NS)	QRS duration (ms)	126 ± 19 vs 143 ± 23 ( <i>P</i> = 0.03)		
		Tricuspid annulus systolic excursion (mm)	14.9 ± 2.5 vs 11.5 ± 3.6 ( <i>P</i> = 0.003)		
		Exercise endurance time (% of predicted mean for age and sex)	84 ± 9 vs 75 ± 14 ( <i>P</i> = 0.04)		
	PVR	0/16 vs 7/20 ( <i>P</i> = 0.03)			
Kaushal <i>et al.</i> (1997), Cardiol Young, India [10]  Prospective randomized controlled trial (level II)	<i>n</i> = 20: transatrial (group 1)	Late mortality	Nil	Limitations: short follow-up; RV function not assessed under stress	
	<i>n</i> = 20: transventricular (group 2)	RVOT gradient (mmHg)	16.79 ± 13.49 vs 12.5 ± 10.12		
	Mean age: 3.09 vs 4.56 years	Significant RV hypokinesia (EF < 30%)	0% vs 15%		
	Follow-up: 6 months	Ventricular arrhythmia	Nil		
Alexiou <i>et al.</i> (2002), Eur J Cardiothorac Surg, UK [4]  Retrospective cohort (level III)	<i>n</i> = 91: transventricular (group 1)	5-, 10- and 20-year survival	97 ± 1% ( <i>P</i> = NS)	Transatrial repair had higher incidence of residual RVOTO and lower freedom from reoperation in infants  Limitations: patients were selected for transatrial repair if transannular patch was predicted	
	<i>n</i> = 69: transatrial (group 2)	Echocardiography: RVOT gradient >40 mmHg	6% vs 18% ( <i>P</i> = 0.03)		
		Mean age: 200.2 vs 188.6 days	Moderate PR		48% vs 28% ( <i>P</i> = 0.007)
		Moderate RV dilatation	32% vs 18% ( <i>P</i> = 0.05)		
	Mean follow-up: 14.5 vs 6 years	Good biventricular function	97% vs 99% ( <i>P</i> = NS)		
		24-hour Holter: Recurrent ventricular tachycardia	1.7% vs 0%		
		Reoperations: 10-year freedom from reintervention	92% ± 3% vs 65% ± 6% ( <i>P</i> < 0.0001)		

Continued

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% (P < 0.0001)	
		10-year freedom from PVR	97% ± 2% vs 100% (P = NS)	
Sun <i>et al.</i> (2013), Asian J Surg, China [11]	n = 53: transatrial-transpulmonary (group A)	Perioperative outcomes:		Limitations: short follow-up; no CMR data available on RV function
Prospective randomized controlled trial (level II)	n = 53: transventricular (group B)  Mean age: 11.53 vs 10.43 months (P = NS)  Mean follow-up: 39.6 months	Cardiopulmonary bypass (min)	95.02 ± 23.8 vs 85.23 ± 22.63 (P = 0.032)	
		Cross-clamp (min)	69.4 ± 10.36 vs 61.17 ± 9.38 (P = 0.035)	
		Inotropic support (days)	1.63 ± 0.97 vs 2.1 ± 1.09 (P = 0.02)	
		Intubation (h)	26.62 ± 12.48 vs 33.02 ± 17.55 (P = 0.033)	
		Intensive care (days)	2.25 ± 1.28 vs 2.85 ± 1.46 (P = 0.026)	
		Perioperative complications:		
		Reoperation	5.7% vs 0% (P = 0.079)	
		Low cardiac output	1.9% vs 9.4% (P = 0.093)	
		Arrhythmias	5.7% vs 18.9% (P = 0.038)	
		Follow-up:		
		Arrhythmias	1.89% vs 14% (P = 0.024)	
		RVOT gradient (mmHg)	12.16 ± 5.56 vs 11.6 ± 6.84 (P = NS)	
		Moderate-to-severe PR	5.66% vs 20% (P = 0.056)	
		Mild-moderate RV dysfunction	0% vs 8% (P = 0.036)	
Lee <i>et al.</i> (2014), J Thorac Cardiovasc Surg, South Korea [2]	n = 39: limited RV-otomy (transatrial) (group 1)	RV EDVi (ml/m <sup>2</sup> )	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 discouraged
Retrospective cohort (level III)	n = 74: conventional RV-otomy (group 2)  Mean age: 1.8 vs 3.3 years (P = 0.007)  Mean interval between repair and CMR: 12.7 vs 17.2 years (P < 0.001)  Mean follow-up: 14.5 vs 21.1 years (P < 0.001)  Propensity score-matched pairs	RV EF	54% ± 9% vs 52% ± 10% (P = NS)	
		Freedom from PVR at 20 years	29.5% ± 14.5% vs 38.1% ± 6.1% (P = NS)	
		Reoperation for RVOTO	0% vs 2.7% (P = NS)	
		Mortality	2.6% vs 0% (P = NS)	
		Arrhythmia	0% vs 2.7% (P = NS)	
		Peak oxygen consumption (ml/kg/min)	29 ± 6 vs 30 ± 6 (P = NS)	
Padalino <i>et al.</i> (2017), J Card Surg, Italy [12]	n = 42: transventricular (group 1)	Any adverse event	42.9% vs 32.4% (P = NS)	Limitations: inter-centre variability; different age and associated procedures; only 26.8% of all patients were studied
Retrospective cohort (level III)	n = 37: transatrial (group 2)	Reoperation	31.0% vs 16.2% (P = NS)	
		PVR	28.6% vs 5.4% (P = 0.033)	

Continued

Table 1: Continued

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
	Median age: 1.0 vs 0.3 years ( $P < 0.001$ )	Peak oxygen uptake (ml/min/m <sup>2</sup> , mean)	31.4 vs 39.5 ( $P = 0.006$ )	
	Median follow-up: 17.8 vs 15.7 years ( $P = NS$ )	CMR (median): RV EDVi (ml/m <sup>2</sup> )	130.15 vs 137.43 ( $P = NS$ )	
	CMR at median 10.5 years after repair	RV EF	50.96% vs 51.23% ( $P = NS$ )	
		PR	31.24% vs 36.43% ( $P = NS$ )	
		Impact of transatrial repair, odds ratio (95% confidence interval):	0.043 (0.005–0.372); $P = 0.004$	
		PVR	0.260 (0.071–0.954); $P = 0.042$	
		Surgical reintervention		
Simon <i>et al.</i> (2019), Semin Thorac Cardiovasc Surg, USA [3]	$n = 21$ : extended RV-otomy (group 1)	Survival	30 years: 93.6% ( $P = NS$ )	Limitations: small sample; non-concurrent periods
	$n = 17$ : limited RV-otomy (group 2)	Freedom from reoperation	10 years: 57.1% vs 94.1% ( $P = 0.02$ )	
Retrospective cohort (level III)	Mean age: 3.8 vs 2.7 years ( $P = 0.001$ )	Ventricular arrhythmias or sup- raventricular tachycardia	25 years: 45% vs 55% ( $P = NS$ ) 20 years: 7% vs 30% ( $P = NS$ )	
	Median follow-up: 30.9 years	Cumulative events (reoperation, arrhythmia or death)	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)	25 years: 54% vs 50% ( $P = NS$ ) 20 years: 9 vs 10 ( $P = NS$ )	
		Maximal oxygen consumption (% predicted, median)	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: $5.82 \pm 1.93$ vs $4.75 \pm 2.30$ ( $P = NS$ ) 30 years: $5.55 \pm 1.69$ vs $4.14 \pm 0.63$ ( $P = 0.03$ )	

Data are presented as mean  $\pm$  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 supraventricular 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 6-months 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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