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Long-term outcomes following transatrial versus transventricular repair on right ventricular function in tetralogy of Fallot

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Abstract

Background and Aim of the Study: Outcomes after repair of tetralogy of Fallot (TOF) are good with either a transventricular (TV) or transatrial (TA) approach. We sought to determine if there is a relationship between the TV or TA approach and right ventricular (RV) function, and the role of residual pulmonary regurgitation (PR) on the long-term outcomes.

Methods: This was a retrospective cohort multicentric study on survivors after surgical repair of TOF (TA versus TV approach, ±transannular patch) between 1990 and 2004. All patients underwent magnetic resonance imaging to assess RV volume, function, and PR. Patients were matched for length of follow-up and age. Clinical adverse events were retrieved from institutional databases.

Results: Seventy-nine patients (TA/TV = 37/42, median age 0.3 and 1.0 yrs, respectively) were included. At a median follow-up of 16.6 years (12.5-20.3), there were no differences in freedom from reintervention (either catheter or surgical), RV volumes, function, and PR between the TA and TV groups. Pulmonary valve (PV) replacement was significantly less frequent in the TA subgroup ($P = 0.033$) and patients with a preserved PV showed significantly lower RV volumes and less adverse events at follow-up.

Conclusions: There is no significant difference in RV volumes and function between the TA and TV. However, the TA approach seems to be protective against PV replacement in the long-term. When PV is not preserved at repair, residual pulmonary regurgitation is a significant cause of late RV dysfunction and dilation, and is associated with a higher rate of late adverse events.

1 | INTRODUCTION

Tetralogy of Fallot (TOF) is the most frequent cyanotic congenital heart disease (CHD) with a prevalence of 3.9 per 10,000 live births.[1] Surgical repair has been evolving[2–4] and outcomes have improved consistently, with current perioperative mortality as low as 1.5%.[3] While the first TOF repair was performed by means of a right ventricle (RV) incision,[2] a transatrial (TA) approach was later introduced to avoid (or minimize) structural damage to the RV and preserve its function.[5,6] Nevertheless, numerous studies have demonstrated excellent early and late results

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with either technique,[6–10] and there is no clear evidence with regard to which approach is associated with better late RV functional outcomes. Recent studies suggest that a trans-annular patch (TAP) with subsequent pulmonary valve regurgitation (PR) can result in decreased long-term RV function.[10,11] For this reason, several authors have focused on surgery for TOF with pulmonary valve (PV) preservation.[12–15]

Cardiac magnetic resonance (CMR) imaging is currently the gold standard for a thorough and complete evaluation of RV morphology and function.[16–19] In view of these issues, we performed a CMR multi center imaging study to evaluate RV function following either transventricular (TV) or TA repair of TOF.

2 | MATERIAL AND METHODS

This is a retrospective, nonrandomized, multicenter CMR study, focused on the evaluation of RV function and dimensions in late survivors after repair of TOF, with either a TA or a TV approach, with or without a TAP in three different centers. Patients undergoing surgery between 1990 and 2004, with a minimum clinical follow-up of 10 years, and at least one CMR study in the last 12 months, were included. Exclusion criteria were: absence of parental informed consent; presence of complex CHD (such as double outlet RV, atrioventricular septal defect, absent PV, or pulmonary atresia); PV implantation (percutaneous or surgical) before CMR; contraindications to perform CMR, such as claustrophobia; presence of previously implanted CMR-incompatible pacemakers (PM); and/or automatic implantable cardioverter defibrillator (ICD), or primary arrhythmias. Patients who did not match for length and age at follow-up were also excluded.

Each local hospital committee on clinical investigation approved the review of medical records. Demographic, intraoperative, and postoperative data were retrieved from each institutional database. Patients were stratified by surgical approach (TA vs TV) and by utilization of a TAP or preservation of PV anatomy and annulus (TAP group vs NoTAP group). Echocardiographic assessment included qualitative 2D evaluation of ventricular dimensions and contractility (mild, moderate, severe degree), and quantification of tricuspid annular plane systolic excursion (TAPSE). A stress test (Bruce protocol) was performed whenever possible, and only the VO2 peak value was recorded for comparison between patients.

Cardiac magnetic resonance assessment was performed on a 1.5-T scanner (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany), and included: electrocardiogram gated, breath-holding balanced steady-state free-precession cine images in four-chamber, two-chamber, left ventricular (LV), and RV outflow tracts views, and short-axis 7-mm contiguous stack of the atrioventricular ring to the apex, from which biventricular volumes, mass, and function were derived. Phase-velocity mapping sequences were acquired in a plane transecting the main pulmonary trunk to calculate PR fraction, expressed as diastolic reversed flow volume/systolic forward flow volume × 100. After acquisition, CMR images were post-processed with a dedicated software (CVI42, Circle Cardiovascular Imaging Inc., Calgary, Canada) by cardiologists with expertise in CMR of CHD. All ventricular volumes (RV and LV end-diastolic [EDV] and end-systolic volumes) were indexed for patient's body surface area; RV function was estimated as reported by Goetschalckx et al.[19]

Adverse events at follow-up included PM/ICD implantation, any surgical reoperation or interventional procedure, and PV replacement (surgical/percutaneous).

2.1 | Surgical techniques

Transatrial repair of TOF included a TA closure (through the tricuspid valve) of the ventricular septal defect (VSD) with a pericardial patch, while right ventricular outflow tract (RVOT) enlargement was performed using a generous myotomy and myomectomy, through the tricuspid annulus. When a PV annulus z score was ≤2 (at intra operative measurement) and a TAP was required, an infundibulotomy <5 mm was utilized.[20] The TV approach consisted of VSD closure through a wide longitudinal RV incision, which could be extended upward through the PV annulus when a TAP was required. A pericardial patch or a mono-cusp homograft patch was used for the TAP,[20] according to each center and surgeon's preference. Whenever PV preservation or sparing techniques were employed, these included valve commissurotomy and/or hegar dilation.

2.2 | Statistical analysis

Statistical analysis was performed using SPSS 23.0 (IBM Corp., Armonk, NY). SAS 9.4 (SAS Institute, Cary, NC) was used for multiple hypothesis testing. Normality for all variables was tested using the Shapiro-Wilk test. Not normal distributed variables were expressed as median with interquartile range. Normally distributed variables were expressed as mean with 95% confidence interval. Categorical and dichotomous variables were expressed with absolute and relative frequencies. Unadjusted differences were compared using the Wilcoxon Sum Rank Test or *t*-test, as appropriate. Differences in categorical variables were compared using Fisher's exact, or ChiSquare test, as appropriate. Survival estimates were plotted using Kaplan-Meier curves. Risk factors in multivariate analysis were tested using the Cox proportional hazard model. Non proportionality of hazards was adjusted including an interaction term computed with follow-up time, where appropriate. Adjusted effects of covariates (gender, age at intervention, previous Blalock Taussig [BT] shunt, and PV preservation) in outcome variables were calculated using logistic (for dichotomous variables) or linear (for continuous variables) regression after propensity score inverse probability weighting, in order to take into account significant differences between both TV versus TA and TAP versus NoTAP subgroups. To compare the means of several correlated endpoints to the covariates surgical approach and PV preservation, we applied multiple hypothesis testing. In particular, we compared the means of the five endpoints (interventional procedures, reoperations, PV replacement, EDV, and PR percentage at magnetic resonance imaging) and obtained adjusted *P*-values, defined as the smallest significance level for which the given hypothesis would be rejected. We used a bootstrap approach to approximate the distribution of the minimum *P*-value of all tests. The bootstrap method is computationally intensive but appealing in that, unlike other methods, correlations and distributional characteristics are incorporated into the adjustments. A *P*-value <0.05 was considered as statistically significant.

3 | RESULTS

Between 1990 and 2004, 815 patients underwent surgical repair for TOF (TV/TA = 573/242): 294 were eligible for the study, but only 79 patients (26.8%, Figure 1) could be included (TV/TA = 42/37). Preoperative and postoperative data are listed in Tables 1 and 2.

When analyzing the TA versus TV approach (Table 1), all the TA repairs were performed in one center. Median age at repair was 0.7 years; however, patients undergoing TA repair were significantly younger (0.3 yrs vs 1 yr, $P < 0.001$); 15 patients (19%) required a BT shunt prior to repair, with no statistical difference between groups.

When analyzing results of TOF repair regardless of the TA versus TV surgical approach (Table 2), the PV was preserved in 18 patients (NoTAP Group; seven had TA repair); the remaining patients required a TAP (TAP group; 30 had TA repair). A mono-cusp pulmonary homograft patch was used in 26 patients, while a valveless pericardial patch was utilized in the remaining patients. No patients undergoing TA repair with PV preservation needed a subpulmonary outflow patch.

Associated surgical procedures at repair were performed in 11 patients (13.9%) and consisted of patch pulmonary artery (PA) plasty in eight patients (right in five, left in one, both in two), patent ductus arteriosus closure in two, and subaortic stenosis resection in one.

The immediate postoperative course was uneventful in all but three patients: two in the TA group required prolonged mechanical ventilation (>48 h); in the TV group, one patient presented with postoperative bleeding causing tamponade and required urgent mediastinal reexploration. All patients were discharged home in good clinical condition; pre-discharge 2D echocardiography showed no significant tricuspid valve regurgitation; PR and RV function were not significantly different between groups. Patients who had PV preservation or TAP with a monocusp showed a tendency toward reduced early PR.

At a median follow-up of 16.6 years (interquartile range [IQR] 12.5-20.3, 100% complete, Table 1), all patients were in New York Heart Association class I-II, with no cardiac medications. All but two patients were in sinus rhythm. One patient (TA group) required PM implantation for sinus bradycardia occurring soon after CMR was done; another one (TV group) presented with paroxysmal supraventricular tachycardia requiring medications.

Adverse events (either catheter or surgical procedures, or both) occurred in 30 patients (12 in TA group, 18 in TV group, $P = 0.341$, Table 1). Nineteen patients (nine in TA group, 10 in TV group, $P = 0.231$) required interventional catheter procedures: PA branch balloon dilation in 11, PA branch stenting in six, and percutaneous PV implantation in two (Medtronic Melody® 20 mm after TA repair,

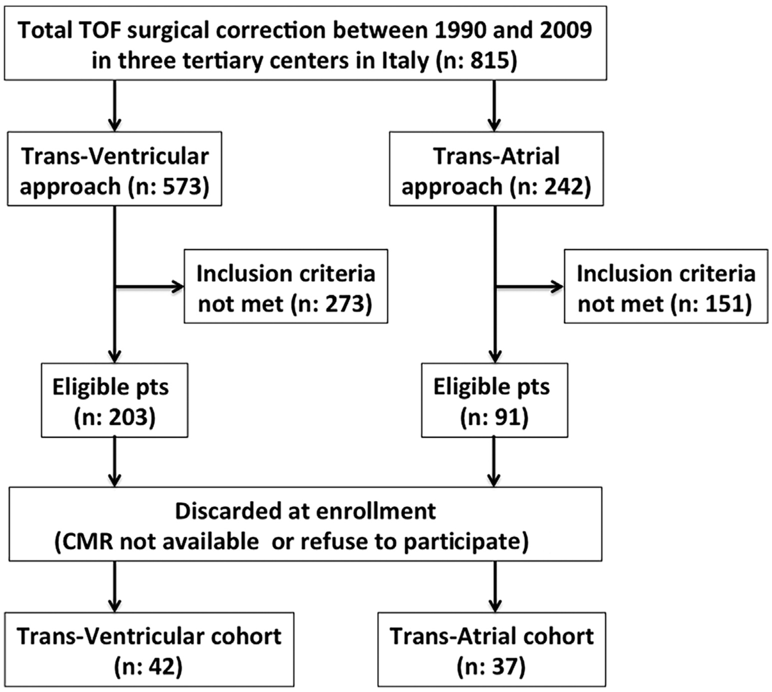

FIGURE 1 Flowchart showing total number of patients operated for tetralogy of Fallot in the considered timeframe in the three centers, and the criteria of selection of the final 79 patients who are the object of this study. CMR, cardiac magnetic resonance; TA, transatrial; TOF, tetralogy of Fallot; TV, transventriculart

TABLE 1 Demographic, operative, and follow-up data in the transventricular versus transatrial repair of tetralogy of Fallot

	Transventricular (*n*:42)	Transatrial (*n*:37)	Total (*n*:79)	*P* value
Operation data				
Age at operation[b] (yrs)	1 (0.6-2.025)	0.3 (0.25-0.75)	0.7 (0.3-1.3)	**<0.001**
Gender (female)[b] (*n*, %)	24/42 (57.1%)	13/37 (35.1%)	37/79 (46.8%)	**0.05**
Year at operation[b]	1995 (1993-1997)	1996 (1995-1997)	1996 (1995-1997)	0.282
BT shunt (*n*, %)	11/42 (26.2%)	4/37 (10.8%)	15/79 (19.0%)	0.082
Associated surgical procedures (*n*, %)	2/42 (4.8%)	9/37 (24.3%)	11/79 (13.9%)	**0.02**
PV preservation (*n*, %)	11/42 (26.2%)	7/37 (18.9%)	18/79 (22.8%)	0.442
Follow-up data				
Total FU[b] (yrs)	17.8 (11.3-21.45)	15.7 (13.3-19.2)	16.6 (12.5-20.3)	0.477
Event-free survival[b] (yrs)	13.2 (10.38-21.025)	13.4 (5.5-17.6)	13.4 (10.3-19)	0.190
Any adverse event (*n*, %)	18/42 (42.9%)	12/37 (32.4%)	30/79 (38.0%)	0.341
Interventional procedures (*n*,%)	10/42 (23.8%)	9/37 (24.3%)	19/79 (24.1%)	0.231*
Re-operation (*n*,%)	13/41 (31.0%)	6/37 (16.2%)	19/79 (24.7%)	0.427*
PV replacement (*n*,%)	12/42 (28.6%)	2/37 (5.4%)	14/79 (17.7%)	0.033*
VO2 peak[a] (mL/min/m2)	31.4 (35.9-43.2)	39.5 (26.6-36.3)	36.2 (33.0-39.4)	**0.006**
TAPSE[b] (mm)	17 (15-19)	17 (15-18)	17 (15-18)	0.633

BT, Blalock Taussig; FU, follow-up; PV, pulmonary valve; TA, transatrial; TAP, transannular patch; TAPSE, tricuspid annular plane systolic excursion.
Data are expressed as: [a]Mean (95% confidence interval), [b]Median (interquartile range).
*Adjusted with multiple hypothesis testing. See text for details.

Medtronic Inc., Minneapolis, MN; Edwards Lifesciences Sapien ®23 mm after TV repair, Edwards Lifesciences, Irvine, CA). Surgical reoperations occurred in 19 patients (24.7%) who had required a TAP repair previously (Table 2), six after TA repair (PV implantation in two), 13 in TV groups (PV implantation in 12). Other reoperations consisted of a combination of RVOT residual obstruction resection in four, PA branch plasty in two, residual VSD closure in one, PM implantation in one.

TABLE 2 Demographic, operative, and follow-up data according to pulmonary valve preservation (no TAP versus TAP) during surgical repair of tetralogy of Fallot

	TAP (*n*:61)	No TAP (*n*:18)	Total (*n*:79)	*P* value
Operation data				
Age at operation[b] (yrs)	0.92 (0.7-1.13)	1.28 (0.63-1.95)	1.0 (0.78-1.21)	0.149
Gender (female) (*n*, %)	27/61 (44.3%)	10/18 (55.6%)	37/79 (46.8%)	0.399
Year at operation[b]	1994 (1992-2000)	1998 (1993-2003)	1996 (1992-2000)	**0.08**
BT shunt (*n*, %)	12/61 (19.7%)	3/18 (16.7%)	15/79 (19.0%)	0.775
Associated surgical procedures (*n*, %)	10/61 (16.4%)	1/18 (5.6%)	11/79 (13.9%)	0.440
Surgical approach TA (*n*, %)	30/61 (49.2%)	7/18 (38.9%)	37/79 (46.8%)	0.442
FU data				
Total FU[b] (yrs)	15.3 (13.0-17.6)	16.9 (15.8-18.0)	16.6 (12.5-20.3)	0.176
Event-free survival[b] (yrs)	13.5 (11.7-15.3)	13.6 (10.9-16.2)	13.4 (10.3-19)	0.980
Any adverse event (*n*, %)	28/61 (45.9%)	2/18 (11.1%)	30/79 (38.0%)	**0.08**
Interventional procedures (*n*,%)	17/61 (27.9%)	2/18 (11.1%)	19/79 (24.1%)	0.139*
Re-operation (*n*,%)	19/61 (31.1%)	0/18 (0.0%)	19/79 (24.1%)	**0.028***
PV replacement (*n*,%)	14/61 (22.9%)	0/18 (0.0%)	14/79 (17.7%)	**0.104**
VO2 peak[a] (mL/min/m2)	34.7 (31.5-38.0)	43.0 (31.6-54.4)	36.2 (33.0-39.4)	0.098
TAPSE[b] (mm)	17 (15-18)	18 (15-18.5)	17 (15-18)	0.678

BT, Blalock Taussig; FU, follow-up; PV, pulmonary valve; TA, transatrial; TAP, transannular patch; TAPSE, tricuspid annular plane systolic excursion.
Data are expressed as: [a]Mean (95% confidence interval), [b]Median (interquartile range).
*Adjusted with multiple hypothesis testing. See text for details.

TABLE 3 Propensity score inverse weighting adjustment for evaluation of impact of a transatrial repair on long-term outcomes

Outcome parameter	Trans-atrial odd ratio	95%CI	*P* value
PV replacement	0.043	0.005-0.372	0.004
Surgical reintervention	0.260	0.071-0.954	0.042
Interventional procedure	0.444	0.119-1.660	0.228
Any reintervention	0.508	0.139-1.856	0.306
RV EDVi >150 mL/mq	0.472	0.148-1.504	0.204

CI, confidence interval; PV, pulmonary valve; RV EDVi, right ventricular end-diastolic volume indexed.

Stress test data were available in 34/79 patients (13 in TA group, 21 in TV). There was a significant difference in VO2 peak measurements when comparing the TA versus TV group (39.5 vs 31.4 mL/min/kg, $P = 0.006$).

Echocardiographic qualitative evaluation showed mild biventricular systolic dysfunction in all patients, with moderate to severe RV dilation; in all patients, TAPSE was not significantly different when comparing TA versus TV groups and NoTAP versus TAP groups (Tables 1 and 2). Pulmonary regurgitation was quantified as mild to moderate in all patients. Mild to moderate tricuspid valve regurgitation was present in most patients, but was not hemodynamically significant.

All subgroups (TV vs TA, Table 1, and NoTAP vs TAP, Table 2) had comparable follow-up ($P = 0.477$ and 0.176, respectively). There were no differences in unadjusted number of interventional procedures at follow-up between the TA and TV groups. However, there was a significantly lower incidence of PV replacement in the TA group ($P = 0.033$, Table 1). In addition, a significantly lower incidence of surgical reinterventions ($P = 0.028$) were observed in unadjusted data in the NoTAP patients (Table 2). There were no surgical reinterventions or PV replacement events in the NoTAP group.

Furthermore, multivariate analysis (using propensity score inverse probability weighting) showed that the TA approach was protective for both PV replacement (odds ratio [OR] = 0.043, $P = 0.004$) and any surgical reintervention (OR = 0.26, $P = 0.042$) (Table 3).

All patients had CMR, after a median time from repair of 10.5 years (IQR 9.6-16.5). Significant RV dilatation was present in both TA and TV groups (Table 4) when compared to range of normality,[19] with a mild reduction of RV ejection fraction, with comparable PR severity, but there was no significant difference between the two groups. However, the NoTAP Group presented with significantly smaller RV volumes ($P = 0.047$) and a trend of smaller PR severity ($P = 0.057$) when compared to the TAP Group (Table 4). There were

TABLE 4 Cardiac magnetic resonance unadjusted data after repair of tetralogy of Fallot according to a surgical approach (transatrial vs transventricular) and utilization of TAP

Parameters	Transventricular (*n*:42)	Transatrial (*n*:37)	Total (*n*:79)	*P* value
RV EDVi[a] (mL/m^2)	130,15 (117,37-42,92)	137,43 (123,35-151,51)	133.5 (124.2-142.8)	0.905*
RV ESVi[a] (mL/m^2)	58,00 (43,50-79,50)	64,00 (48,00-80,00)	60.50 (46.5-79.75)	0.524
RV EF[b] (%)	50,96 (49,02-52,91)	51,23 (48,47-53,98)	51.1 (49.5-52.7)	0.871
LV EDVi[a] (mL/m^2)	81,00 (71,50-94,00)	75,00 (67,00-86,00)	78.5 (70.5-89.0)	0.153
LV ESVi[a] (mL/m^2)	35,00 (27,50-48,50)	33,50 (27,75-38,00)	34.0 (27.5-41.5)	0.489
LV EF[a] (%)	58,00 (53,00-63,50)	58,00 (55,00-62,00)	58.00 (54.25-62.75)	0.703
PR[a] (%)	31,24 (24,71-37,77)	36,43 (31,04-41,82)	33.63 (29.38-37.89)	0.644*
	TAP (*n*:61)	**NoTAP (*n*:18)**	**Total (*n*:79)**	
RV EDVi[a] (mL/m^2)	139,80 (128,94-150,65)	111,65 (97,22-126,07)	133.5 (124.2-142.8)	**0.047***
RV ESVi[a] (mL/m^2)	66,00 (52,00-80,00)	48,00 (40,00-57,50)	60.50 (46.5-79.75)	**0.008**
RV EF[b](%)	50,39 (48,53-52,23)	53,49 (50,20-56,79)	51.1 (49.5-52.7)	0.109
LV EDVi[a] (mL/m^2)	78,50 (69,50-90,00)	81,00 (71,50-86,00)	78.5 (70.5-89.0)	0.940
LV ESVi[a] (mL/m^2)	34,00 (28,50-39,75)	34,00 (26,50-46,50)	34.0 (27.5-41.5)	0.928
LV EF[a] (%)	58,00 (53,75-60,50)	58,00 (54,50-66,00)	58.00 (54.25-62.75)	0.520
PR.[a] (%)	36,55 (31,85-41,25)	24,22 (15,13-33,32)	33.63 (29.38-37.89)	**0.057***

EDV, end-diastolic volume; EDVi, EDV indexed; EF, ejection fraction; ESV, end-systolic volume; ESVi, ESV indexed; LV, left ventricle; PR, pulmonary regurgitation; RV, right ventricle; TAP, transannular patch.

Data are expressed as: [a]Mean (95% confidence interval), [b]Median (interquartile range).

*Adjusted with multiple hypothesis testing. See text for details.

TABLE 5 Predictors of RV volumes and pulmonary regurgitation at multivariate analysis

Cardiac magnetic resonance parameter and predictor	Multivariate *P* value	Beta coefficient	95%CI
RV EDVi			
Transatrial approach	0.832	–	
Pulm valve preservation	0.033	−0.259	(−49.7;−2.1)
Age at intervention	0.463	–	
Gender	0.114		
Previous BT shunt	0.039	−0.249	(−49.7;−1.3)
RV ESVi			
Transatrial approach	0.692	–	
Pulm valve preservation	0.059	−0.241	(−31.3;0.6)
Age at intervention	0.434	–	
Gender	0.254		
Previous BT shunt	0.086	–	
RV PR%			
Transatrial approach	0.412	–	
Pulm valve preservation	0.007	−2.77	(−23.2;−3.8)
Age at intervention	0.220	–	
Gender	0.088		
Previous BT shunt	0.016	−0.285	(−22.4;−2.8)

BT, Blalock Taussig; EDVi, end-diastolic volume indexed; ESVi, end-systolic volume indexed; PR, pulmonary regurgitation; RV, right ventricle.

no significant differences in LV dimensions and function among all groups.

At multivariate analysis (Table 5), PV preservation and previous BT shunt were independent predictors of reduced indexed end-diastolic RV volumes (RV EDV indexed, *P* = 0.033, and *P* = 0.039), and milder PV regurgitation (*P* = 0.007 and *P* = 0.016).

When comparing TA versus TV groups, there were no significant differences in freedom from adverse events (Figure 2A) or PV replacement (Figure 2B). However, survival analysis shows that events occurred mostly within the first 5 years in the TA group, with a low late attrition; on the contrary, the TV group showed a constant attrition during the entire length of follow-up (Figure 2A). This is also evident in the multivariate analysis (Table 6) with the Cox model: since the proportionality of hazard assumption is not met, a time-varying HR is present, with a significantly higher risk of adverse events in the TA group in the first 5 years of follow-up, that gradually decrease and finally equalize with the TV group at 10 years. On the contrary, TA was a significantly protective factor from PV replacement (hazard ratio = 0.084, *P* = 0.029) on multivariate analysis. Since there were no events in the NoTAP group, PV preservation was not included in the model.

When comparing TAP versus NoTAP groups (preserved PV), there was a significantly higher occurrence of adverse events (Figure 3A) and of PV replacement (Figure 3b) in TAP patients. However, on multivariate analysis TAP did not emerge as an independent predictor of adverse events.

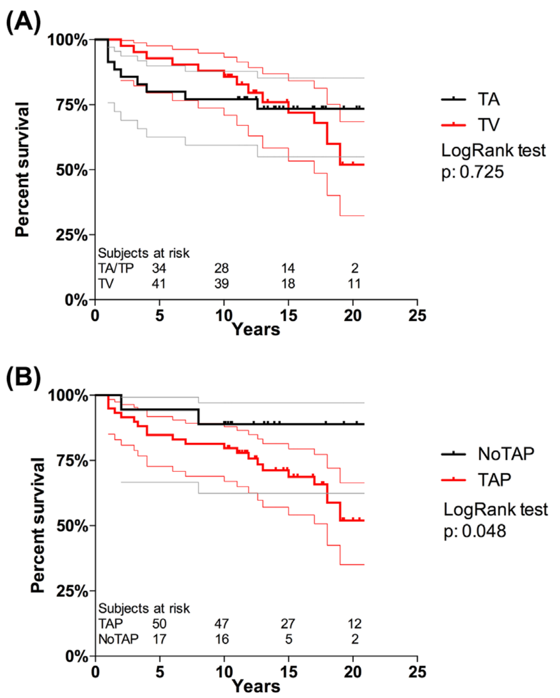

FIGURE 2 Freedom from adverse events, according to surgical approach (TA vs TV) (Figure A), and to TAP versus no TAP (Figure B). Curves are showed in solid bold lines. Confidence intervals are showed in solid thin lines. TA, transatrial; TAP, transannular patch; TV, transventricular

TABLE 6 Multivariate survival analysis: Cox regression

	Multivariate *P* value	Hazard ratio	95%CI
Pulmonary-free survival			
TA approach	0.029	0.084	(0.01-0.77)
Age at intervention	0.190	0.537	(0.21-1.36)
Gender (female)	0.098	0.282	(0.06-1.26)
Previous BT shunt	0.232	0.364	(0.07-1.92)
Event free survival			
TA approach[a]	<0.001		
1 year		138.0	(15-1238)
2 years		77.8	(10-572)
5 years		13.9	(2.96-65.6)
10 years		0.79	(0.15-4.16)
TA approach* FU time[1]	<0.001		
Pulmonary valve preservation	0.738	0.74	(0.13-4.2)
Age at intervention	0.436	1.21	(0.75-1.98)
Gender (female)[a]	0.086	0.291	(0.105;0.806)
Gender (female)* FU time[1]	<0.001		
1 year		4.1	(0.71-23.8)
2 years		3.3	(0.63-17.3)
5 years		1.7	(0.42-6-83)
10 years		0.57	(0.19-1.67)
15 years		0.19	(0.07-0.56)
Previous BT shunt	0.081	0.38	(0.13-1.13)

BT, Blalock Taussig; FU, follow-up; TA, transatrial.
[a]Proportional hazard assumption not met (since interaction term computed with time of follow-up result statistically significant). Hazard ratio is time varying, so hazard rations at 1,2,5,10, 15 years of FU are shown. See methods section for further details.

4 | DISCUSSION

This study was designed to identify whether a TA or a TV surgical approach to repair TOF could significantly affect clinical outcomes and long-term RV size and function. We could not find any significant difference in RV dimensions or function between the TA and TV groups. However, preservation of PV function was associated with significantly smaller RV volumes and better RV function.

Continuous improvement in surgical techniques and postoperative management have made surgical repair of TOF feasible in early infancy with a low mortality.[3] Conventional TV repair of TOF that involves a longitudinal surgical incision of the RV, large enough to close the VSD, is currently a common procedure,[3] while TA repair is thought to be superior in early and long-term results, since the RV geometry may be preserved.[6–8] Critics of the TA approach state that despite the minimal longitudinal RV incision, myocardial damage still occurs since the RV outflow tract is extensively resected to alleviate RVOT obstruction.[7–9] Miura et al[21] investigated RV function by regional wall motion analysis and by global function in 62 patients after repair for TOF, and concluded that the TA repair provided better postoperative global RV function, with less impaired regional wall motion than in the TV approach. However, no reliable data on RV chamber dimensions and clinical outcomes were provided, and PR was not studied. Similarly, Atallah-Yunes et al[9] reported long-term echocardiographic follow-up in two groups of patients after either TA or TV repair, concluding that despite similar residual RVOT stenosis and obligatory PR, RV size was smaller in the TA group, and RV systolic function was more impaired in the TV group.

Cardiac magnetic resonance is now the gold standard modality for assessment of late RV volumes and function.[16,17] Lee et al[22] directly compared long-term outcomes after TA or TV repair with CMR imaging, and showed no differences in chamber dimensions, PR severity, and freedom from PV replacement. They speculated that after TA repair of TOF, both utilization of a TAP and extensive RVOT muscle bundle resection might contribute significantly to late RV dilatation and dysfunction. d'Udekem d'Acoz et al[23] compared 44 patients with PV stenosis repair with no RV damage and preserved RV infundibulum contractility, with 189 patients who had undergone the TV repair of TOF, and concluded that PR is not the only determinant of late RV dilation, and RVOT surgical damage plays an important role in causing RV dilation and symptoms.

In our series, when comparing TA and TV groups of patients matched for follow-up length, age, and anatomic diagnosis, we

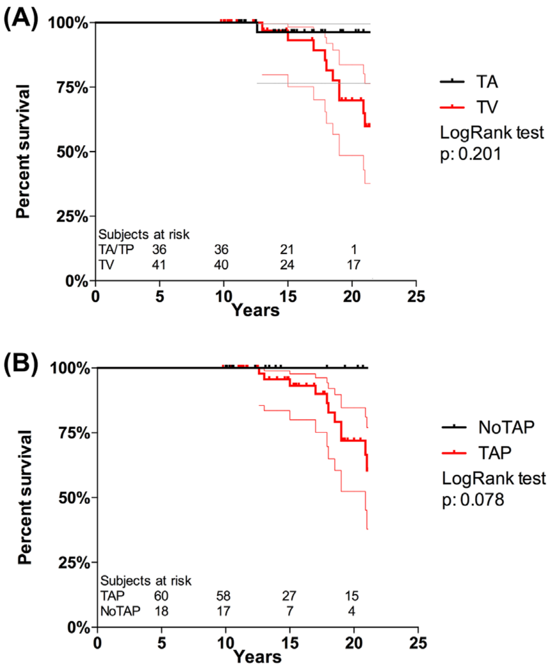

FIGURE 3 Freedom from pulmonary valve replacement, according to surgical approach (TA vs TV) (Figure A), and to TAP versus no TAP (Figure B). Curves are showed in solid bold lines. Confidence intervals are showed in solid thin lines. TA, transatrial; TAP, transannular patch; TV, transventricular

found no significant differences in RV volumes or PR severity in the long-term.

It is of note that adverse events (mostly interventional procedures) were more frequent in the TA group in the first years of follow-up (Figure 2A). This may be related to the different postoperative management policy of the only center which performed TA repair. However, the rate of PV replacement in the TA group at follow-up was significantly reduced (Figure 2B). As expected, this difference seems to be more evident after 10-15 years of follow-up, since in the first 10 years the rate of clinical events was very low. Thus, our data show that the TA surgical approach to TOF repair may reduce the incidence of long-term adverse events in TOF patients.

The use of a TAP is known to be associated with increased PR on long-term follow-up. Alexiou and coworkers,[11] in a series of 160 patients, 77.5% with TAP, reported a better freedom from PV replacement in patients without TAP. Sasson et al[24] reported that RVOT reconstruction with a monocusp improves short-term outcomes and limits postoperative PR. More recently, van den Berg et al[25] showed that 59 TA patients (71% TAP) had progressive RV dilatation and ventricular dysfunction during follow-up. Lee et al[22] reported that PR fraction was an independent predictor of RV dilatation and dysfunction. These studies suggest that utilization of TAP during surgical correction play a significant role in postoperative TOF pathophysiology. Our data also suggest that the utilization of a TAP causes progressive PR after repair, and has a negative impact on both RV dilatation and dysfunction, leading to a higher incidence of adverse events at follow-up. A combination of PR severity and RVOT damage may play the major role in the repaired TOF pathophysiology.

In our study, BT shunt placement was an independent predictor of smaller RV volumes and reduced PR at follow-up. This would appear to contrast with the current policy of early TOF repair (ie, within 4-6 months of age). Early repair is justified by the necessity of minimizing progressive RV hypertrophy and, consequently, avoiding a major RVOT resection and RV damage following repair. However, it may be that delayed surgical repair, provided by BT shunt placement, may enhance the possibility of a physiological growth of a native hypoplastic but not dysplastic PV, so that at time of surgery, a better repair of the PV can be achieved.

5 | STUDY LIMITATIONS

This imaging study has some limitations. First, as a multicenter study, there is a substantial intercenter variability despite the fact that all three centers had extensive experience in performing TOF repairs. Second, the TA and TV groups differed in median ages at repair, and associated concomitant procedures (such as PV annulus preserving strategy that was not uniform during the study period). Third, only 26.8% of all TOF repair patients were studied introducing the possibility of selection bias. Finally, data adjustment for each center was not feasible since only one center (Padua) routinely performed the TA approach for TOF.

6 | CONCLUSION

Our study shows that the TA approach and PV preservation at the time of TOF repair decrease the incidence of long-term PV replacement. Preserving PV function and minimizing PR at the time of the original TOF repair decreases late RV dysfunction and the incidence of adverse clinical events.

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CONFLICT OF INTEREST

None.

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