Article published online: 2022-06-25

Long-Term Results after Fallot Repair

Jonas Markus Kleinöder[1] Ariawan Purbojo[1] Robert Blumauer[1] Michela Cuomo[1] Muhannad Alkassar[2] Sven Dittrich[3] Robert Cesnjevar[4]

[1] Department of Pediatric Cardiac Surgery, Friedrich-Alexander-University Erlangen-Nuremberg (FAU), Erlangen, Germany
[2] Department of Pediatric Cardiology, Erlangen University Hospital, Erlangen, Germany
[3] Department of Pediatric Cardiology, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Germany
[4] Department of Pediatric Cardiac Surgery Universitäts-Kinderspital Zürich, Zurich, Switzerland

Address for correspondence Jonas Markus Kleinöder, Universitätsklinikum Erlangen, Wöhrstraße 17 Erlangen, Erlangen, Bayern 91054, Germany (e-mail: jonaskleinoder@gmail.com).

Thorac Cardiovasc Surg 2022;70:e7–e14.

Abstract

Background The aim of this study was to evaluate the long-term outcome and freedom from pulmonary valve replacement (PVR) after initial repair of tetralogy of Fallot (TOF).

Patients and Methods The cohort of 306 patients treated between 1980 and 2017 was divided into anatomical subgroups according to the diagnosis of TOF-pulmonary stenosis, TOF-pulmonary atresia and TOF-double outlet right ventricle. Patients were treated with transannular patch (TAP), valve sparing repair (VSR), or conduits from the right ventricle to the pulmonary arteries (RVPA conduits).

Results There were 21 deaths (6.9%), 14 being hospital deaths (4.6%) after primary correction and four deaths (1.3%) occurred after PVR. One patient died after a non-cardiac operation (0.3%). There were two late deaths (0.7%). During the past 12 years no early mortality has been observed. Ninety-one patients (30.4%) received PVR after a median of 12.1 ± 7.0 years with an early mortality of 4.4% ($n = 4$) and no late mortality. A significant difference in freedom from reoperation after TAP, VSR, and RVPA-conduits could be identified. Multivariate analysis displayed transannular repair ($p = 0.016$), primary palliation ($p < 0.001$), the presence of major aortopulmonary collateral arteries (MAPCA; $p = 0.023$), and pulmonary valve Z-scores < -4.0 ($p = 0.040$) as significant risk factors for PVR.

Conclusion TOF repair has a beneficial long-term prognosis with low morbidity and mortality. Pulmonary valve Z-scores < -4.0, transannular repair, and presence of MAPCAs are associated with earlier PVR. Non-VSRs and TOF-pulmonary atresia lead to earlier reoperation but have no negative impact on survival.

Keywords
- surgery
- incisions
- tetralogy of Fallot
- reoperation
- outcomes
- pulmonary valve replacement

Introduction

Tetralogy of Fallot (TOF) is a cyanotic congenital cardiac defect named after the French physician Étienne-Louis Fallot, who described its morphology after performing autopsies with right ventricular outflow tract obstruction (RVOTO), ventricular septal defect (VSD), overriding aorta, and hypertrophy of the right ventricle.[1–3] Surgical treatment, however,

received
November 23, 2021
accepted after revision
April 4, 2022

DOI https://doi.org/10.1055/s-0042-1749098.
ISSN 0171-6425.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

was not possible until 1944 when Blalock and Taussig first palliated patients with a systemic to pulmonary artery shunt (Blalock-Taussig-Thomas-shunt).[4] Ten years later, Lillehei performed the first successful surgical repair using cross-circulation,[5] followed by Kirklin's approach using a cardiopulmonary bypass circuit.[6] Before, survival rates were around 50% over the first year of life and only few patients reached adulthood.[7] TOF is the most common form of cyanotic heart diseases, with a prevalence of approximately 3.9 cases per 10,000 live births.[8] Cyanosis and symptoms are determined by the degree of RVOTO and can range from asymptomatic patients to severe hypoxemia.[2] Surgical TOF treatment has changed the prognosis of Fallot patients positively toward survival into adulthood for the majority of all repaired individuals. Several strategies and technical impacts have changed over the course of more than 60 years of surgical history.

The purpose of this retrospective study was to evaluate the long-term results and freedom from pulmonary valve replacement (PVR) from a large historical patient cohort after the initial repair of TOF at our institution. PVR becomes necessary when significant pulmonary regurgitation and RV-dilatation occur.[9] Extensive studies showed a higher risk for PVR after transannular RVOT reconstruction. However, long-term survival for any chosen type of repair is described as excellent.[10–12]

This report analyzes the influences of different surgical techniques on the long-term need of PVR regarding the implication of transannular patch repair (TAP), valve sparing repair (VSR), and primary placement of valved right ventricle to the pulmonary artery conduit (RVPA conduit) with respect to the anatomical variations of the disease, ranging from tetralogy of Fallot-pulmonary stenosis (TOF-PS), TOF-pulmonary atresia (TOF-PA) toward TOF-double outlet right ventricle type (TOF-DORV).

Materials and Methods

Patients

Hospital records and operative protocols of all patients who underwent complete TOF repair at our institution (Erlangen University Hospital) between April 1980 and June 2017 were reviewed. Patients with absent pulmonary valve syndrome and pulmonary atresia-major aortopulmonary collateral arteries (MAPCAs) with complete absence of central pulmonary arteries were excluded. A total of 306 patients entered the retrospective study and were analyzed. The patient cohort was divided into anatomical subgroups according to their pathologic features like TOF-PS ($n = 228$), TOF-PA ($n = 23$), and TOF-DORV($n = 55$). There were 174 males and 132 females, median age and weight at the time of complete repair were 13.5 months (range: 2.6–156.8 months) and 8.5 kg (range: 3.0–40.0 kg). Patient characteristics examined included age at repair, weight, *Z*-scores of the pulmonary valve, primary palliative shunt procedures, presence of MAPCAs, time on cardiopulmonary bypass, aortic cross clamping time, genetic disorder and coronary anomalies. Patient's characteristics for the subgroups are summarized in ►**Table 1**. Information was obtained from medical records and direct contact to outpatient physicians. Late death was

Table 1 Patients characteristics by diagnosis

	TOF-PS	Range	TOF-PA	Range	TOF-DORV	Range
N (%)	228 (74.5)		23 (7.5)		55 (18.0)	
VSR (*n*, %)	138 (60.5)		6 (22.2)[b]		21 (38.2)	
TAP (*n*, %)	87 (38.2)		8 (34.8)		30 (54.5)	
RVPA-conduit (*n*, %)	3 (1.3)		9 (39.1)		4 (7.2)	
Age (months ± SD)	20.7 ± 1.7	2.7–156.8	35.4 ± 6.6	3.9–97.8	17.4 ± 3.1	2.7–141.2
Age <6 mo (months ± SD)	44 ± 14.4		4 ± 1.3		16 ± 5.2	
Sex (male, %)	134 (58.8)		14 (60.9)		26 (47.3)	
Weight (kg ± SD)	9.6 ± 0.3	3.3 − 40.0	12 ± 1.4	5.4–29.5	8.3 ± 0.6	3.0–33.0
Z-Score PV (± SD)	−2.2 ± 0.2		−4.8 ± 0.9		−3.20 ± 0.4	
Primary palliation (*n*, %)	56 (24.6)		20 (87.0)		25 (45.5)	
Additional palliation (*n*, %)	11 (4.8)		4 (17.4)		6 (10.9)	
MAPCAS (*n*, %)	15 (6.6)		6 (22.2)		2 (3.6)	
CPB (min ± SD)	136.0 ± 3.1	53 − 347	192.4 ± 13.4	123–386	184.9 ± 9.3	80–344
ACC (min ± SD)	70.6 ± 1.8	17–172	86.5 ± 6.5	38–171	91.5 ± 6.7	30–234
Chromosomal anomaly[a] (*n*, %)	30 (13.2)		4 (17.4)		11 (20.0)	
Coronary anomaly (*n*, %)	25 (11.0)		4 (17.4)		10 (18.2)	

Abbreviations: ACC, aortic cross clamping; CPB, cardiopulmonary bypass; MAPCAS, major aortopulmonary collateral arteries; PV, pulmonary valve; RVPA-conduit, conduit from the right ventricle to the pulmonary arteries; TAP, transannular patch; VSR, valve saving repair.
[a]Chromosomal anomalies included Trisomy-21 (17), DiGeorge syndrome (5), VACTERL syndrome (9), six microdeletion 22q11 (6), and others (8)
[b]RVOT muscle bundles (septal and parietal band) were divided. RVOT muscle resection was limited to the lowest possible extent.

confirmed after contacting health insurances and governmental registers. Institutional ethics board approval was sought and a waiver of consent obtained.

Operative Technique

All patients underwent repair using hypothermic cardiopulmonary bypass. Deep hypothermic circulatory arrest was rarely needed for surgery ($n = 5$; 1.6%). Median cardiopulmonary bypass time and median aortic cross clamping time were 135.5 minutes (range: 53–386 minutes) and 69.0 minutes (range: 17–234 minutes), respectively. Surgical anatomy and operative complexity, partly represented by total time on bypass and aortic cross-clamping are listed in ►**Table 1**.

Surgical approaches were individually adopted to the patient's anatomy. Whenever possible, incisions did not cross the pulmonary valve annulus. The pulmonary valve orifice was always probed followed by a valvuloplasty to maximize the aperture. Commonly a combination of commissurotomy and leaflet shaving was performed. Surgical delamination of severely hypertrophic valves was adopted late as additional valve sparing technique in 2016.

We aimed to achieve an annulus size close to the normal *Z*-score larger than −2. Most VSDs were repaired from the right atrium through the tricuspid valve. Decisions whether to patch the infundibulum or not were based on the final RVOT dimension. Patches were inserted through an infundibular incision extending to the pulmonary annulus but not crossing it whenever pulmonary valve dimensions were adequate (*Z*-score larger than −2). In the presence of severe pulmonary valve hypoplasia, a transannular patch reconstruction became necessary. Different RVOT-patch materials were used according to surgeon's personal preference. A persistent foramen ovale was closed whenever necessary.

The RVOT was reconstructed with a transannular patch in 125 patients (40.9%), the pulmonary valve annulus was preserved in 165 patients (53.9%) and 16 patients (5.2%) were treated primarily with a RVPA conduit. Patients characteristics according to the type of RVOT repair are described in ►**Table 2**.

Statistical Analysis

The research dataset was compiled during 2016 to 2018. Patient research datasets were extracted from digital and paper-based clinic information systems and patient records and transferred to a prepared EXCEL 2016 (Microsoft, Redmond, Washington, United States) database. Group data are presented as the mean and standard deviation for continuous variables, and proportional data are presented with their 95% confidence interval. Descriptive statistics for comparisons between groups were made using the unpaired *t*-test, Fisher's exact test or univariate analysis of variance (ANOVA), Kaplan-Meier methods with log-rank test and Cox proportional hazards regression analysis were used to analyze long-term survival and freedom from reoperation. Univariate and multivariate regression analyses were used for risk-factor analysis regarding mortality or later PVR. All statistical analyses were undertaken using SPSS 21 statistical software (IBM, Armonk, New York, United States).

Results

Mortality and Survival

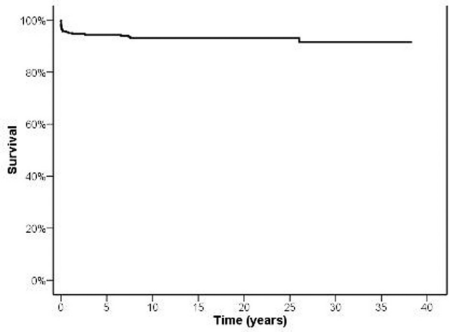
Complete case notes of 306 patients were reviewed and analyzed. Overall mean follow-up time was 16.9 ± 9.7 years

Table 2 Patients' characteristics by type of RVOT repair

	VSR	Range	TAP	Range	RVPA- Conduit	Range
N (%)	165 (53.9)		125 (40.9)		16 (5.2)	
TOF-PS (*n*, %)	138 (83.6)		87 (69.6)		3 (18.8)	
TOF-PA (*n*, %)	6 (3.6)[b]		8 (6.4)		9 (56.3)	
TOF-DORV (*n*, %)	21 (12.7)		30 (24.0)		4 (25.0)	
Age (months ± SD)	20.9 ± 2.0	2.6–156.8	18.6 ± 1.8	2.8–143.1	44.8 ± 11.7	5.3–154.7
Age <6 mo (months ± SD)	34 ± 11.1		28 ± 9.2		2 ± 0.7	
Sex (male, %)	104 (63.0)		63 (50.4)		7 (43.8)	
Weight (kg ± SD)	9.6 ± 0.4	3.0–40.0	9.0 ± 0.4	3.8–30.0	12.5 ± 2.3	4.7–30.0
Z-score PV (± SD)	−1.6 ± 0.2		−3.6 ± 0.2		−5.6 ± 1.1	
Primary palliation (*n*, %)	45 (27.2)		40 (32.0)		16 (100.0)	
MAPCAS (*n*, %)	10 (6.1)		9 (7.2)		4 (25.0)	
CPB (min ± SD)	135.2 ± 3.7	53–347	157.3 ± 5.2	70–344	231.9 ± 1.6	144–386
ACC (min ± SD)	71.3 ± 2.1	19–172	78.9 ± 3.7	17–234	94.7 ± 7.0	42–154
Chromosomal anomaly[a] (*n*, %)	15 (9.1)		26 (20.8)		4 (25.0)	
Coronary anomaly (*n*, %)	20 (12.1)		14 (11.2)		5 (31.2)	

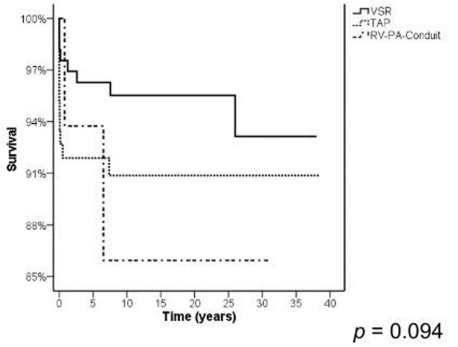
Abbreviations: ACC, aortic cross clamping; CPB, cardiopulmonary bypass; MAPCAS, main aortopulmonary collateral arteries; PV, pulmonary valve; RVPA-conduit, conduit from the right ventricle to the pulmonary arteries; TAP, transannular patch; VSR, valve saving repair.
[a]Chromosomal anomalies included Trisomy-21 (17), DiGeorge syndrome (5), VACTERL syndrome (9), six microdeletion 22q11 (6) and others (8).
[b]Membranous atresia. RVOT muscle bundles (septal and parietal band) were divided. RVOT muscle resection was limited to the lowest possible extent.

(A)



Year	5	10	15	20	25	30
Survival	94.3%	93.1%	93.1%	93.1%	93.1%	91.6%
N. at Risk	246	205	164	114	76	24

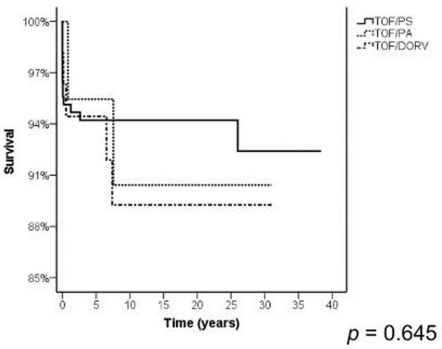
(B)



$p = 0.094$

Year	5	10	15	20	25	30
VSR (n = 165)	96.3%	95.5%	95.5%	95.5%	95.5%	93.1%
N. at Risk	136	114	94	71	52	18
TAP (n = 125)	91.9%	90.9%	90.9%	90.9%	90.9%	90.9%
N. at Risk	98	81	64	38	21	4
RVPA-Conduit (n = 16)	93,8%	85,9%	85.9%	85,9%	85.9%	85.9%
N. at Risk	12	10	6	5	3	1

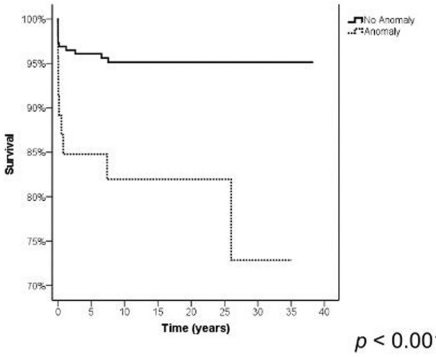
(C)



$p = 0.645$

Year	5	10	15	20	25	30
TOF-PS (n = 228)	94.2%	94.2%	94.2%	94.2%	94.2%	92.4%
N. at Risk	187	159	135	101	67	22
TOF-PA (n = 23)	95.5%	90.4%	90.4%	90.4%	90.4%	90.4%
N. at Risk	19	16	12	6	5	1
TOF-DORV (n = 55)	94.4%	89.3%	89.3%	89.3%	89.3%	89.3%
N. at Risk	40	29	17	7	4	1

(D)



$p < 0.001$

Year	5	10	15	20	25	30
No anomaly (n = 261)	96.1%	95.1%	95.1%	95.1%	95.1%	95,1%
N. at Risk	214	180	143	99	67	19
With anomaly (n = 45)	84.8%	82.0%	82.0%	82,0%	82.0%	72,9%
N. at Risk	32	25	21	15	9	5

Fig 1. Survival (A) Overall survival; (B) comparison between valve saving repair, transannular patch and conduits from the right ventricke to the pulmonary arterys; (C) comparison between TOF- pulmonary stenosis, TOF- pulmonary atresia and TOF- double outlet right ventricle; (D) comparison between patients with chromosomal anomaly and without

Fig. 1 Survival. (**A**) Overall survival; (**B**) comparison between valve saving repair, transannular patch, and conduits from the right ventricle to the pulmonary arteries: (**C**) comparison between TOF pulmonary stenosis, TOF-pulmonary atresia, and TOF-double outlet right ventricle; (**D**) comparison between patients with chromosomal anomaly and without.

(range: 40 days–38.3 years) and for patients with later PVR 19.7 ± 7.9 years (range: 15 months–38.3 years). There was a total of 21 deaths (6.9%), 14 of them being hospital deaths (4.6%) after primary correction, including 11 patients (3.6%) before 30 days after repair. Additional four patients (1.3%) died after PVR. One patient (0.3%) died after a non-cardiac operation and there were two late deaths (0.7%) after 2.6 and 7.3 years with no previous PVR. Causes of late death were sudden heart failure and intractable arrhythmia. However, during the past 12 years, no early mortality following primary repair has been observed. Primary palliation and transannular repair were no risk factors for early death. On univariate and multivariate analysis, only chromosomal anomalies ($p < 0.001$) were associated with a higher mortality, which in detail was related to the patients with Trisomy-21 ($p < 0.001$). VACTERL syndrome ($p = 0.592$), DiGeorge syndrome ($p = 0.981$), and microdeletion 22q11 ($p = 0.199$) were not associated with a higher risk. The overall survival rates stayed high even after 25 and 30 years after repair with 93.1, and 91.6%, respectively (►**Fig. 1A**). No differences in survival distribution were observed for TOF-PS versus TOF-PA and TOF-DORV ($p = 0.645$) or TAP versus VSR and RVPA-conduit ($p = 0.094$) according to the log-rank test (►**Fig. 1**B, C). Significant differences were only present for patients with chromosomal anomalies with a 20- and 30-years survival of 82.0 and 72.9% versus 95.1 and 95.1% for patients without chromosomal anomaly ($p < 0.001$; ►**Fig. 1D**).

Freedom from Pulmonary Valve Replacement

PVR became necessary in 91 out of 306 patients (29.7%) after a mean of 12.1 ± 7.0 years (range: 8 days–30.2 years) after severe symptoms like arrythmia, significant reduced right ventricular ejection fraction or QRS duration >160 milliseconds occurred. Hospital mortality was 4.4% ($n = 4$), three patients died early (3.3%) after PVR and one patient later after 5 months, respectively. All censored patients were in critical condition prior to PVR, which became urgently necessary shortly after primary correction. No late mortality after elective PVR was observed. Overall freedom from PVR was 20.4 ± 1.8 years with 94.0, 83.9, 68.0, 52.8, 44.0, and 33.9% of the patients not needing PVR at 5, 10, 15, 20, 25, and 30 years, respectively (►**Fig. 2A**). The type of repair at the time of complete correction showed a significant difference in freedom from PVR ($p < 0.001$). Median time for TAP was 17.0 ± 2.2 years, for VSR 25.7 ± 3.5 years and for RVPA conduits 10.9 ± 1.0 years ($p < 0.001$). VSR had the longest freedom from PVR with 94.3, 86.9, 77.2, 62.8, 54.8, and 43.7% after 5, 10, 15, 20, 25, and 30 years, respectively as shown in ►**Fig. 2B**. Diagnosis significantly influenced freedom from PVR, TOF-PS patients required surgery after a median of

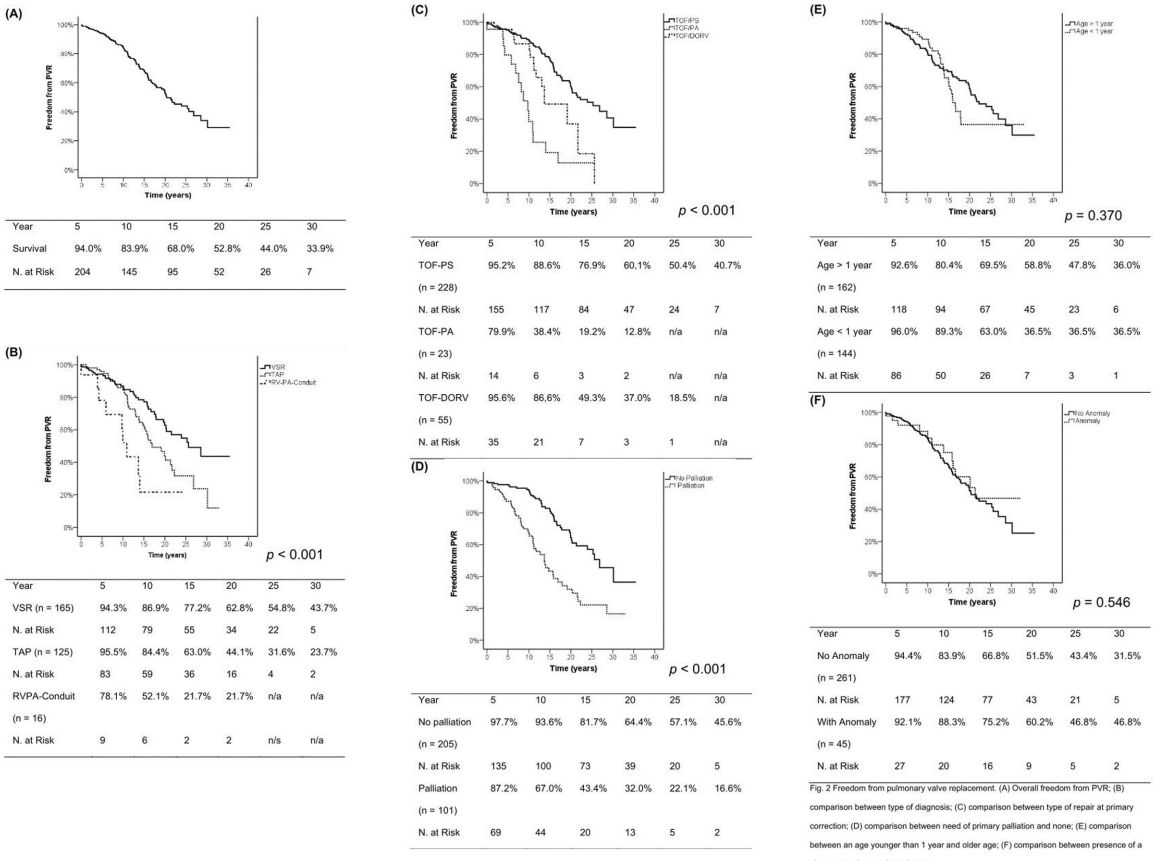


Fig. 2 Freedom from pulmonary valve replacement. (**A**) Overall freedom from PVR; (**B**) comparison between the types of diagnosis; (**C**) comparison between the types of repair at primary correction; (**D**) comparison between the need of primary palliation and none; (**E**) comparison between an age younger than 1 year and older age; (**F**) comparison between the presence of a chromosomal anomaly and none.

25.3 ± 3.1 years, compared with patients with TOF-PA 9.8 ± 1.5 years and TOF-DORV 13.7 ± 2.8 years (p <0.001). Patients with TOF-PS had the longest freedom from PVR with 95.2, 88.6, 76.9, 60.1, 50.4, and 40.7% after 5, 10, 15, 20, 25, and 30 years, respectively as shown in ►**Fig. 2C**. Primary palliation significantly influenced freedom from PVR (p <0.001) being 13.7 ± 1.5 years compared with 26.9 ± 2.3 years for patients without palliation. Freedom from PVR was 97.7, 93.6, 81.7, 64.4, 57.1, and 45.6% after 5, 10, 15, 20, 25, and 30 years, respectively as shown in ►**Fig. 2D**. Primary palliation was most common in patients with TOF-PA (87.0%) followed by TOF-DORV (45.5%) and TOF-PS (24.6%) (►**Table 1**). However, age at the time of repair below 1 year compared with the remaining patients (p = 0.370) and the presence of chromosomal anomalies (p = 0.546) were not associated with a significant higher hazard for PVR (►**Fig. 2E**, F). On univariate analysis, TOF-PA (p <0.001), transannular repair (p = 0.003), small Z-scores for the pulmonary valve (p <0.001), the need of primary palliation prior to total repair (p <0.001), presence of MAPCA (p <0.001), and longer time on cardiopulmonary bypass (p <0.001) were risk factors associated with PVR. Multivariate analysis displayed transannular repair (p = 0.016), primary palliation (p <0.001) and the presence of MAPCA (p = 0.023) as significant risk factors for PVR (►**Table 3**). Pulmonary valve Z-scores below −4.0 were a significant risk factor (p = 0.040) on multivariate analysis, while significant differences already occurred at Z-scores below −3.0 on univariate analysis (p = 0.009). Pulmonary valve Z-scores were significantly smaller in patients who underwent TAP and repair with a conduit than VSR (p <0.001) and a major risk factor for patients diagnosed with TOF-PA requiring RVPA-conduit repair (►**Table 1**, 2).

Discussion

Since the first successful TOF-repair by Lillehei and colleagues in the 1950s, outcomes have significantly improved, with excellent long-term survival and low risks for late sudden death.[12–14] However, long-term studies after TOF-repair have all shown frequent need for PVR due to progressive pulmonary valve regurgitation, right ventricular dysfunction, and decreased functional capacity.[15–17] There has been a growing enthusiasm for TOF repair techniques implying preservation of the pulmonary valve and its annulus, thus prolonging time until PVR.[12] Historical series confirm that late PVR is significantly less common whenever the annulus remained intact. However, whether all forms of valve preservation translate into late clinical advantages is difficult to prove.[11,18]

Operative mortality has constantly decreased with rates currently close to 0% even in neonates and young infants,[19] supporting our own surgical results with no early mortality since 2004. Previous studies[19,20] including patients who underwent total repair of TOF in the earlier era of Fallot repair report that younger age at the time of operation, lower weight, and transannular patch reconstruction were risk factors for death. Several improvements over time like mechanical properties and materials used for cardiopulmonary bypass, surgical timing, surgical indication, and the surgical techniques itself have dramatically improved since the early years of Fallot repair. These factors most certainly became less relevant. Our series identified Trisomy-21 as an independent risk factor with negative impact on survival, despite the low number of only 16 cases (5.2%). This might be explained by a potentially higher pulmonary vascular resistance level and narrow airways commonly found in patients

Table 3 Risk factors for PVR

	Univariate	Multivariate		
	p	p	OR	CI (95%)
PA	0.000	0.052	1.890	0.994–3.594
DORV	0.062			
Transannular repair	0.003	0.016	1.732	1.106–2.711
Age <6 mo	0.860			
Weight (kg)	0.062			
Z-score PV	0.000	0.239	1.306	0.838–2.037
Z-score < −4.0	0.000	0.040	1.691	1.025–2.79
Primary palliation	0.000	0.000	2.434	1.534–3.862
Additional palliation	0.197			
MAPCA	0.000	0.023	2.236	1.116–4.480
CPB (min)	0.000	0.187	1.003	0.998–1.009
ACC (min)	0.826			
Chromosomal anomalies	0.547			
Coronary anomaly	0.112			

Abbreviations: ACC, aortic cross clamping; CI, confidence interval; CPB, cardiopulmonary bypass; DORV, double outlet right ventricle; MAPCAS, main aortopulmonary collateral arteries; OR, odds ratio; PA, pulmonary atresia; PV, pulmonary valve.

with Trisomy-21, which possibly influences early and late outcomes. In conjunction to this, some other series have been showing that genetic syndromes are associated with poorer survival.[13]

The overall survival in our cohort was excellent despite the long observational period. There were no significant differences between the different observed groups TOF-PS, TOF-PA, and TOF-DORV, discordant to the previous results of other authors showing poorer late survival in the TOF-PA group.[15,18,21] This might be partially explained by the smaller number of patients in this cohort and the fact that pulmonary atresia with absent central pulmonary arteries and only MAPCAs were not included in this study. In addition, there was no significant differences between TAP, VSR, and repair via RVPA-conduit for mortality. Therefore, it seems that preserving the pulmonary annulus does not improve late survival necessarily. These findings align with previous studies.[13,14] Also, no early mortality during the past 12 years of the study was observed, which predicts an even better result if the series is repeated in the future.

Progressive pulmonary valve regurgitation is a frequent indication for re-operation in this patient group after surgical reconstruction. Right ventricular enlargement and distension, further tricuspid regurgitation and later dysfunction of both ventricles, ventricular arrhythmia including sudden death are potential sequela and complications that need to be addressed.[13,22,23] Despite several risk factors, reoperative mortality rates stay constantly low.[17] Historically, PVR has been necessary in more than 50% of late survivors. Some reports suggested poorer survival and an increased frequency of pulmonary regurgitation after total repair of TOF using a transannular patch.[24] In our series, 125 patients (40.9%) received TAP and there was a significant difference in the freedom from reoperation between the patients who underwent VSR, TAP, and repair with a RVPA-conduit. Higher reintervention rates for RVPA-conduits are a common fact, as conduits get obstructed due to their limited growth potential.[25] Preoperatively, pulmonary valve *Z*-scores, intraoperative pulmonary valve anatomy have been used to determine whether the annulus could be preserved or not. *Z*-scores of the pulmonary valve larger than −2 and non-dysplastic pulmonary valve leaflets were considered factors that made preservation of the pulmonary annulus possible.

In addition, anatomical variations have been reported to be a significant risk factor for reintervention and later PVR.[15,16] Our study included 23 patients with TOF-PA and 55 patients with TOF-DORV. Abovementioned subgroups needed PVR much earlier in comparison to patients with TOF-PS. These findings completely agree with previous reports,[15,16,21] although the small number of patients in those subgroups must be considered. Overall freedom from PVR rate was 94.0, 83.9, 68.0, 52.8, 44.0, and 33.9% after 5, 10, 15, 20, 25, and 30 years, respectively. Initial palliation prior to total repair is known to be associated with earlier PVR,[10,14,26] which we could confirm in our study data as well. Small diameters for the pulmonary valve and RVOT are probably the underlying reason to explain this fact, leading often to TAP in these patients.[18,27] In our study, *Z*-scores below −4.0, use of transannular patch, and presence of MAPCAs affected the freedom from PVR significantly. Further PVR was needed even after VSR, as the repaired valves are probably far different from normal function. However, if PVR becomes necessary, it will be after a longer period in these patients. Small diameters of the pulmonary valve annulus led to more frequent palliation and more frequent need of TAP. Also, the presence of MAPCAs indicates higher pulmonary resistance due to collateral flow, smaller pulmonary arteries, and rather small pulmonary valve annulus due to lesser antegrade RVOT-flow.

This study was limited by its retrospective nature and the inclusion of patients operated during a wide-ranging period, with an enormous technical and pathophysiological impact on surgery and postoperative care. Only completely recovered patients at our institution were included in this series. The parameters used to evaluate surgical risk factors were subjective. One important limitation is that the late sequela of TOF repair typically take decades to manifest. It is therefore impossible to draw firm conclusions regarding the very late risk of PVR so far.

Conclusion

TOF repair has up to date a completely beneficial long-term prognosis with low morbidity and low mortality. Presence of Down syndrome was negatively associated with survival. PVR is a frequently needed second operation with a considerable low risk, even in the setting with multiple previous operations. Primary palliative procedures, pulmonary valve *Z*-scores < -4.0, transannular repair, and presence of MAPCAs are associated with earlier PVR. Non-VSRs and TOF-PA lead to earlier reoperation but have no negative impact on survival. In general, surgical preservation of the pulmonary annulus with several current techniques like pulmonary valve delamination can reduce reoperation rates.

Note

The present work was performed in fulfillment of the requirements for obtaining the degree "Dr. med Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU)."

Conflict of Interest

None declared.

References

1 Fallot E-LA. Contribution à l'anatomie pathologique de la maladie bleue (cynose cardiaque). Marseille Méd 1888;25:77–93
2 Al Habib HF, Jacobs JP, Mavroudis C, et al. Contemporary patterns of management of tetralogy of Fallot: data from the Society of Thoracic Surgeons Database. Ann Thorac Surg 2010;90(03):813–819, discussion 819–820
3 Starr JP. Tetralogy of fallot: yesterday and today. World J Surg 2010;34(04):658–668
4 Blalock A, Taussig HB. Landmark article May 19, 1945: the surgical treatment of malformations of the heart in which there is pulmonary stenosis or pulmonary atresia. By Alfred Blalock and Helen B. Taussig. JAMA 1984;251(16):2123–2138
5 Lillehei CW, Cohen M, Warden HE, et al. Direct vision intracardiac surgical correction of the tetralogy of Fallot, pentalogy of Fallot,

and pulmonary atresia defects; report of first ten cases. Ann Surg 1955;142(03):418–442
6 Kirklin JW, Dushane JW, Patrick RT, et al. Intracardiac surgery with the aid of a mechanical pump-oxygenator system (gibbon type): report of eight cases. Proc Staff Meet Mayo Clin 1955;30 (10):201–206
7 Bertranou EG, Blackstone EH, Hazelrig JB, Turner ME, Kirklin JW. Life expectancy without surgery in tetralogy of Fallot. Am J Cardiol 1978;42(03):458–466
8 Talner CN. Report of the New England Regional Infant Cardiac Program. Pediatrics 1998;102(1 Pt 2):258–259
9 Ferraz Cavalcanti PE, Sá MP, Santos CA, et al. Pulmonary valve replacement after operative repair of tetralogy of Fallot: meta-analysis and meta-regression of 3,118 patients from 48 studies. J Am Coll Cardiol 2013;62(23):2227–2243
10 Lee CH, Kwak JG, Lee C. Primary repair of symptomatic neonates with tetralogy of Fallot with or without pulmonary atresia. Korean J Pediatr 2014;57(01):19–25
11 Kim GS, Han S, Yun TJ. Pulmonary annulus preservation lowers the risk of late postoperative pulmonary valve implantation after the repair of tetralogy of Fallot. Pediatr Cardiol 2015;36(02):402–408
12 Blais S, Marelli A, Vanasse A, et al. Comparison of long-term outcomes of valve-sparing and transannular patch procedures for correction of tetralogy of Fallot. JAMA Netw Open 2021;4(07): e2118141
13 Mizuno A, Niwa K. Transannular patch repair remains popular: the reasons for choosing the transannular patch should be discussed. Eur J Cardiothorac Surg 2015;47(06):1112
14 Ylitalo P, Nieminen H, Pitkänen OM, Jokinen E, Sairanen H. Need of transannular patch in tetralogy of Fallot surgery carries a higher risk of reoperation but has no impact on late survival: results of Fallot repair in Finland. Eur J Cardiothorac Surg 2015;48(01):91–97
15 Knott-Craig CJ, Elkins RC, Lane MM, Holz J, McCue C, Ward KE. A 26-year experience with surgical management of tetralogy of Fallot: risk analysis for mortality or late reintervention. Ann Thorac Surg 1998;66(02):506–511
16 Ducas RA, Harris L, Labos C, et al. Outcomes in young adults with tetralogy of Fallot and pulmonary annular preserving or transannular patch repairs. Can J Cardiol 2021;37(02):206–214
17 Van den Eynde J, Sá MPBO, Vervoort D, et al. Pulmonary valve replacement in tetralogy of Fallot: an updated meta-analysis. Ann Thorac Surg 2022 Mar;113(03):1036–1046 vvb
18 Park CS, Lee JR, Lim HG, Kim WH, Kim YJ. The long-term result of total repair for tetralogy of Fallot. Eur J Cardiothorac Surg 2010;38 (03):311–317
19 Menaissy Y, Omar I, Mofreh B, Alassal M. Total correction of tetralogy of Fallot in the first 60 days of life in symptomatic infants: is it the gold standard? Thorac Cardiovasc Surg 2020;68 (01):45–50
20 Sarris GE, Comas JV, Tobota Z, Maruszewski B. Results of reparative surgery for tetralogy of Fallot: data from the European Association for Cardio-Thoracic Surgery Congenital Database. Eur J Cardiothorac Surg 2012;42(05):766–774, discussion 774
21 Ganigara M, Sagiv E, Buddhe S, Bhat A, Chikkabyrappa SM. Tetralogy of Fallot with pulmonary atresia: anatomy, physiology, imaging, and perioperative management. Semin Cardiothorac Vasc Anesth 2021;25(03):208–217
22 Graham TP Jr. Management of pulmonary regurgitation after tetralogy of Fallot repair. Curr Cardiol Rep 2002;4(01):63–67
23 Cheung EW, Wong WH, Cheung YF. Meta-analysis of pulmonary valve replacement after operative repair of tetralogy of fallot. Am J Cardiol 2010;106(04):552–557
24 Kirklin JK, Kirklin JW, Blackstone EH, Milano A, Pacifico AD. Effect of transannular patching on outcome after repair of tetralogy of Fallot. Ann Thorac Surg 1989;48(06):783–791
25 Balasubramanya S, Zurakowski D, Borisuk M, et al. Right ventricular outflow tract reintervention after primary tetralogy of Fallot repair in neonates and young infants. J Thorac Cardiovasc Surg 2018;155(02):726–734
26 Kwak JG, Shin HJ, Bang JH, et al. Effect of pulmonary valve replacement in the repaired tetralogy of Fallot patients with trans-annular incision: more than 20 years of follow-up. Korean Circ J 2021;51(04):360–372
27 Schneider C, McCrindle BW, Carvalho JS, Hornberger LK, McCarthy KP, Daubeney PE. Development of Z-scores for fetal cardiac dimensions from echocardiography. Ultrasound Obstet Gynecol 2005;26(06):599–605