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Long-Term Survival in Patients With Repair of Tetralogy of Fallot: 36-Year Follow-Up of 490 Survivors of the First Year After Surgical Repair

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Objectives. **We sought to analyze risk factors for long-term survival (up to 36 years) after surgical repair of tetralogy of Fallot (TOF).**

Background. **Survival after repair is excellent, but data >20 years are rare.**

Methods. **From 1958 to 1977, 658 patients underwent correction of TOF at our institution and were analyzed for survival. Of this patient group (age 12.2 ± 8.6 years [mean ± SD], range 2 to 67), 39.7% had a previous palliation. Operative (n = 139) and 1-year (n = 29) deaths were excluded for long-term calculations, resulting in a study group of 490 patients.**

Results. **Actuarial 10-, 20-, 30- and 36-year survival rates were 97%, 94%, 89% and 85%, respectively. Mortality increased 25 years postoperatively from 0.24%/year to 0.94%/year (p = 0.003). The most common cause of death was sudden death (n = 13), followed by congestive heart failure (n = 6). Multivariate correlates of impaired long-term survival were date of operation (before 1970, p = 0.0104), preoperative polycythemia (p = 0.0487) and use of a right ventricular (RV) outflow patch (p = 0.0079). Postoperative systolic RV/left ventricular pressure ratio and age showed no influence. Patients without preoperative polycythemia and an RV outflow patch (n = 164) had a 36-year actuarial survival rate of 96% and normal life expectancy.**

Conclusions. **Cyanosis, operative experience of the surgeon and an RV outflow tract patch influence long-term outcome after repair of TOF in older children. Early repair by experienced surgeons to avoid polycythemia and excessive RV hypertrophy is supported by this study. However, mortality risk increases 25 years postoperatively, and thus heart monitoring should be intensified.**

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On August 31, 1954, Walton C. Lillehei attempted the first operative correction of tetralogy of Fallot (TOF), the most common cause of cyanotic congenital heart disease (1). Since that time, operative mortality has decreased dramatically, and correction is now usually performed in infancy or early childhood (2). Thus, the adverse long-term effects of cyanosis and chronic hypoxia are avoided, but the use of an outflow tract patch is more common in some centers (3). Long-term survival is reported to be excellent but still lower than that of the normal population (4). However, it remains uncertain whether these results last for a lifetime and whether subgroups of patients may achieve normal life expectancy (5).

This study reviews our historic (1958 to 1977) long-term experience in the correction of TOF and pulmonary stenosis in 739 patients. Correction was performed predominantly in children 10 years old, and previous palliation was common. The large patient group is homogeneous because mainly all patients were operated on by one surgeon (W.K.) using the same technique, without changes in operative management. Therefore, risk factors can be analyzed in large subgroups in which significant differences can be demonstrated. Special attention was paid to the factors that are believed to influence long-term survival: age at the time of operation, the presence of earlier palliative operation, the degree of preoperative cyanosis, the need for and type of outflow tract enlargement and the postoperative right ventricular/left ventricular (RV/LV) systolic pressure ratio.

Methods

Patients. From December 1958 to May 1977, 739 patients with the diagnosis of TOF with pulmonary stenosis underwent complete surgical repair at the Clinic of Cardiac Surgery at the University of Munich. This period was chosen because only a single surgeon (W.K.) had operated on the vast majority of these patients, minimizing differences in surgical technique. Patients with other complex congenital heart lesions were excluded (e.g., pulmonary atresia, double-outlet RV). We

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Abbreviations and Acronyms

ASD = atrial septal defect
AV = atrioventricular
ECC = extracorporeal circulation
HCT = hematocrit
LV = left ventricle, left ventricular
PFO = patent foramen ovale
RV = right ventricle, right ventricular
TOF = tetralogy of Fallot

attempted to contact all patients who survived the immediate postoperative period. We were unable to locate 16 of them (follow-up complete in 98%), but information from the German Resident Registry (Einwohnermeldeamt) indicated that they were alive at least 12 years after the operation. All foreigners (n = 52), as well as those known to have moved outside of Germany (n = 13), were excluded from follow-up. Figure 1 shows the overall survival of these patients. To analyze the factors that influence long-term survival, we excluded the steep, nonlinear, first phase of the survival curve. The curve becomes linear after 1 year; therefore, all patients who died within the 30-day (n = 139 [19%]) and 1-year (n = 29 [4%]) postoperative period were separated for further long-term survival analyses. Table 1 shows a survey of patient characteristics, including concomitant heart malformations and previous palliative operations.

Operative methods. All operations were performed using extracorporeal circulation (ECC) and moderate hypothermia (28° to 30°C). In the first operations, a Kay-Gärtner screen oxygenator was used, which was replaced in later procedures by a Travenol or Bentley bubble oxygenator. The intracardiac correction was performed through a horizontal RV incision. However, if the decision was made to use an outflow tract patch, a vertical incision was made. Outflow tract patches were used in either the subvalvular (preserving pulmonary valve competence) or transvalvular (including splitting of the valvular ring) position. A concomitant patent foramen ovale (PFO) was left open while all other accompanying defects were corrected (including a type II atrial septal defect [ASD II]). During the intracardiac maneuver, the aorta remained clamped for 24 ± 10 min (mean ± SD); the average bypass time was 52 ± 16 min. A cardioplegic solution was not used in any of the procedures.

Follow-up and statistical methods. Follow-up was conducted between 1994 and 1995 and consisted of a written questionnaire. In cases where the patient did not answer repeated letters, telephone interviews were used. We asked the patients about their functional status, the occurrence of cardiovascular events (stroke, transient ischemic events, myocardial infarction, infective endocarditis, arrhythmias, pacemaker implantation, cardiac catheterization and reoperation), concomitant diseases, hospital admittance, use of drugs, physical activity and occupational status. If a patient died, the closest living relative and the patient's physician were contacted to evaluate the cause of death.

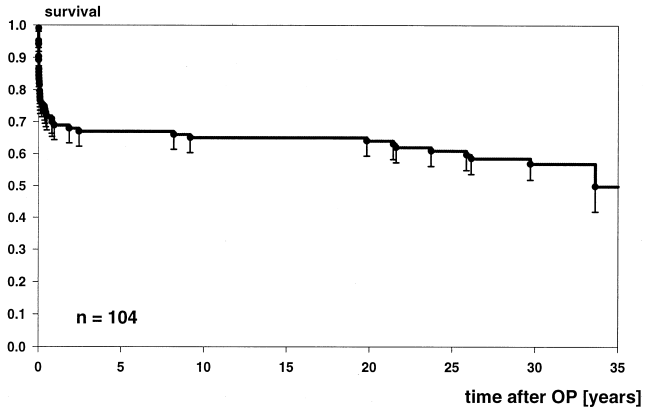

Figure 1. Survival after correction of TOF. The first, steep phase of the survival curve lasts ~1 year. After that time, the curve becomes linear. **Each step in the curve** denotes an event, and at each event the standard error is indicated by **vertical bars.** OP = operation.

To calculate the influence of variables on operative and 1-year survival, univariate comparisons were carried out using the two-tailed chi-square test with the Yates correction for discrete variables. Whenever necessary, the Fisher exact test was used. Multivariate analyses were performed by multivariate analysis of variance.

Table 1. Preoperative Data

	All Pts (n = 658)	30-Day Survivors (n = 519)	1-Year Survivors (n = 490)
Age (yr)	12.2 ± 8.6	12.1 ± 8.2	11.8 ± 8.0
Weight (kg)	31.0 ± 16.6	31.5 ± 16.7	30.6 ± 15.2
Height (cm)	133 ± 21.9	134 ± 21	134 ± 21
Female	45%	44%	45%
Preop HCT (%)	54 ± 12	53 ± 12	53 ± 12
Preop erythrocytes (10^6/dl)	6.0 ± 2.62	5.76 ± 1.76	5.72 ± 1.78
Prev palliative op			
Modified B-T shunt	188 (29.4%)	140 (26.9%)	136 (27.8%)
Central shunt	11 (1.7%)	7 (1.3%)	6 (1.2%)
Brock's op	65 (10.2%)	56 (10.8%)	51 (10.4%)
1 prev op	231 (36.1%)	175 (33.7%)	166 (33.9%)
2 prev op	22 (3.4%)	16 (3.1%)	15 (3.1%)
3 prev op	1 (0.2%)	1 (0.2%)	0
Concomitant cardiac malformations			
ASD I	1 (0.2%)	0	0
ASD II	65 (10.2%)	51 (9.8%)	45 (9.2%)
PFO	129 (20.2%)	112 (21.5%)	108 (22%)
Situs inversus	4 (0.8%)	3 (0.6%)	3 (0.6%)
Left SVC	20 (3.1%)	12 (2.3%)	12 (2.4%)
Multiple VSD	2 (0.4%)	0	0

Data presented are mean value ± SD or number (%) of patients. ASD = atrial septal defect; B-T = Blalock-Taussig; HCT = hematocrit; op = operation, operations; PFO = patent foramen ovale; Preop = preoperative; Prev = previous; Pts = patients; SVC = superior vena cava; VSD = ventricular septal defect.

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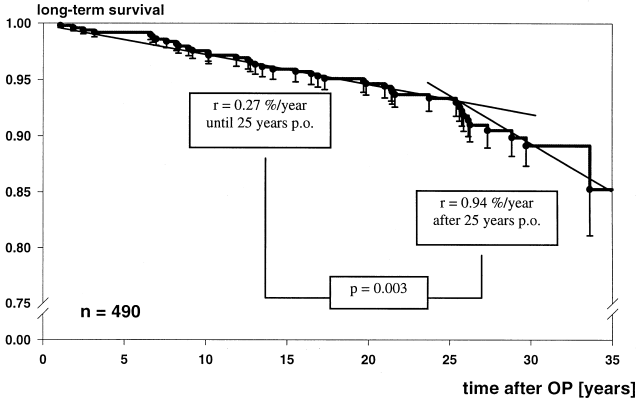


Figure 2. Long-term survival after correction of TOF. All patients who died within the first year after correction were excluded for calculation of long-term survival. The curve shows two different phases that are distinct. The early, low risk phase lasts 25 years; thereafter, the risk increases significantly. Mortality risk (r) per year, as a linearized number, is calculated for each phase. Note the break in the y axis. OP = operation; p.o. = postoperatively.

The probability of long-term survival was estimated using the Kaplan-Meier method. Differences between groups were calculated by the log-rank test. The survival curve was compared with the expected curves of persons of the same age and gender born at the same time, as derived from the Landesamt für Statistik of Bavaria, Germany. The association of variables to long-term survival was first tested in an univariate model. Every univariate variable reaching or approaching significance ($p < 0.1$) was then tested in a Cox multivariate model and removed stepwise if no significant influence was proved. Statistical analyses were facilitated with the help of SPSS statistical software (SPSS Inc.).

Results

Overall survival. The mean duration of follow-up was 25.3 years (median 25.4, range 1.06 to 35.5). Actuarial 10-, 20-, 30- and 36-year survival rates in the 490 patients who survived the first postoperative year were 97%, 94%, 89% and 85%, respectively. Long-term survival was excellent but still significantly lower than that in the normal population ($p < 0.001$). Mortality was linear in the first 25 years after the operation and equaled 0.24% per year. Thereafter, it increased significantly to 0.94%/year ($p = 0.003$) (Fig. 2). During the long-term follow-up period, 42 patients died, most from cardiac causes (n = 26 [62%]). Table 2 describes the causes of late death and the time of their occurrence in detail.

Analysis of risk factors. Many preoperative and postoperative factors were tested for whether they influenced operative and 1-year mortality or late survival. Table 3 shows the most important results for short-term survival. Univariate correlates of adversely affected long-term survival included use of an pulmonary outflow patch ($p = 0.0002$), longer duration of cardiopulmonary bypass ($p = 0.023$), presence of an ASD II ($p = 0.017$), preoperative polycythemia ($p = 0.036$), no palliative operation ($p = 0.046$) and date of operation (better outcome for patients operated on in the 1970s; $p = 0.026$). On multivariate analysis, only date of operation ($p = 0.0104$), preoperative polycythemia ($p = 0.0487$) and use of a pulmonary outflow patch ($p = 0.0079$) correlated with the outcome. Table 4 shows the results of univariate and multivariate analyses of long-term survival.

Survival according to age at operation. Survivors of the first year were classified into four age categories: <6 years old at date of operation (n = 46); 6 to 10 years old (n = 240); 11 to 20 years old (n = 139); and >20 years old (n = 64). Their 35-year survival rates were 91.3%, 91.9%, 87.8% and 72.1%

Table 2. Causes of Death During Long-Term Survival

	No. (%) of Pts Who Died	Pt Age at Death (yr)	Postoperative Death (mo)
Cardiac causes	26 (61.9%)		
Sudden cardiac death	15 (35.7%)	13, 15, 15, 18, 21, 22, 24, 25, 32, 33, 34, 34, 34, 37, 45	38, 83, 91, 98, 110, 122, 153, 156, 162, 169, 256, 305, 307, 346
CHF	6 (14.3%)	13, 13, 17, 28, 37, 64	13, 22, 30, 79, 122, 356
MI	2 (4.8%)	59, 65	260, 403
RV aneurysm	1 (24%)	34	309
Reoperation	1 (2.4%)	21	203
Recurrent VSD	1 (2.4%)	22	107
Noncardiac causes	8 (19%)		
Suicide	2 (4.8%)	19, 35	151, 327
Sepsis	2 (4.8%)	75	238
Brain abcess	1 (2.4%)	27	252
Pneumonia	1 (2.4%)	75	284
Stroke	1 (2.4%)	20	142
Kidney failure	1 (2.4%)	15	80
Unknown*	8 (19%)	19, 25, 27, 29, 41, 44, 59, 66	100, 186, 198, 207, 257, 310, 314, 426

*In two patients, suicide was likely but not confirmed. CHF = congestive heart failure; MI = myocardial infarction; Pt = patient; RV = right ventricular; other abbreviations as in Table 1.

Table 3. Risk Factors for Short-Term Survival

Variable*	Definition of Groups I to IV	Data Available (n)	Operative Mortality (n = 658)						1-Year Mortality (n = 658)					
			I (%)	II (%)	III (%)	IV (%)	Univariate p Value	Multivariate p Value	I (%)	II (%)	III (%)	IV (%)	Univariate p Value	Multivariate p Value
Age	(I) ≤10 vs. (II) >10 yr	658	19.3	18.3			0.74		22.1	25.1			0.37	
Gender	(I) female vs. (II) male	658	20.0	17.9			0.5		22.5	23.9			0.69	
Preop NYHA class	**I vs. II vs. III vs. IV**	**657**	**0**	**3.8**	**16.1**	**46.4**	**<0.001**	**<0.001**	**0**	**9.4**	**19.4**	**57.1**	**<0.001**	**<0.001**
Preop polycythemia	*(I) HCT ≤48% vs. (II) 49–60% vs. (III) >60%*	*643*	*11.0*	*20.2*	*25.7*		*<0.001*		*15.0*	*23.9*	*32*		*<0.001*	
PFO	**(I) no PFO vs. (II) PFO**	**658**	**20.0**	**13.2**			**0.063**	**0.006**	**25.1**	**14.1**			**0.034**	**0.006**
ASD II	(I) no ASD II vs. (II) ASD II	658	18.6	21.5			0.57		22.5	30.8			0.13	
Multiple VSD or ASD I	**(I) no malformation vs. (II) malformation**	**658**	**18.7**	**100**			**0.024**	**0.003**	**23.1**	**100**			**0.036**	**0.014**
Left SVC	**(I) no left SVC vs. (II) left SVC**	**651**	**18.4**	**40**			**0.036**	**0.006**	**23.0**	**40.0**			**0.10**	**0.033**
Situs inversus	(I) no situs inversus vs. (II) situs inversus	658	18.9	25			0.75		23.3	25.0			0.94	
Modified B-T shunt	**(I) no shunt vs. (II) shunt**	**658**	**16.2**	**25.5**			**0.006**	**0.014**	**21.5**	**27.7**			**0.094**	
Central shunt	(I) no shunt vs. (II) shunt	657	18.5	36.4			0.13		22.8	45.5			0.14	
Brock's op	(I) no Brock vs. (II) Brock	658	19.5	13.8			0.27		23.5	21.5			0.72	
Prev palliative op	(I) no previous palliation vs. (II) palliation	657	15.3	24.4			0.009		19.8	28.7			0.009	
VSD size	(I) ≤20 vs. (II) >20 mm	524	18.2	18.9			0.83		20.7	26.3			0.14	
Outflow tract patch	**(I) no patch vs. (II) subvalvular patch vs. (III) transvalvular patch**	**658**	**15.9**	**17.5**	**32.7**		**<0.001**	**0.032**	**20.0**	**20.0**	**37.3**		**<0.001**	
Degree of hypothermia	*(I) <28° vs. (II) >28°C*	*619*	*23.3*	*13.4*			*0.003*		*26.4*	*19.0*			*0.037*	
Bypass time	**(I) ≤40 vs. (II) >40 min**	**646**	**6.6**	**22.6**			**<0.001**	**<0.001**	**8.4**	**28.0**			**0.001**	**<0.001**
Date of op	(I) before 1970 vs. (II) 1970 and after	658	19.1	18.8			0.93		23.1	23.6			0.89	
Postop RV/LV SBP	*(I) ≤0.5 vs. (II) >0.5*	*585*	*15.0*	*20.8*			*0.069*		*17.8*	*26.7*			*0.01*	

*Significant influence on survival is indicated by italic (univariate analysis) or boldface type (multivariate analysis). LV = left ventricular; NYHA = New York Heart Association; postop = postoperative; SBP = systolic blood pressure; other abbreviations as in Tables 1 and 2.

Table 4. Risk Factors for Long-Term Survival

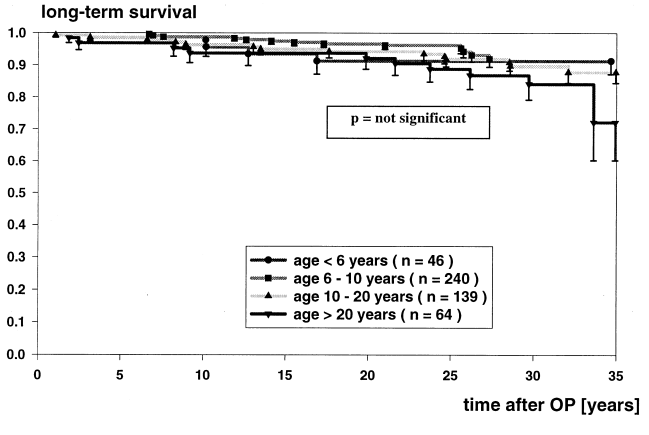
Variable*	Definition of Groups	Favorable Long-Term Survival	Data Available (n)	Long-Term Survival (n = 490) Univariate p Value	Long-Term Survival (n = 490) Multivariate p Value
Age	≤10 vs. >10 yr	Younger	490	0.072	
Gender	Female vs. male	Female	490	0.147	
NYHA class preop	I vs. II vs. III vs. IV		489	0.48	
Preop polycythemia	**HCT ≤48 vs. >48 mg/dl**	**HCT ≤48 mg/dl**	**481**	**0.036**	**0.049**
PFO	No PFO vs. PFO		490	0.95	
ASD II	*No ASD II vs. ASD II*	*No ASD II*	*490*	*0.017*	
Left SVC	No left SVC vs. left SVC		483	0.94	
Situs inversus	No situs inversus vs. situs inversus		490	0.58	
Prev palliative op	*No previous palliation vs. palliation*	*Previous palliation*	*489*	*0.046*	
Modified B-T shunt	No shunt vs. shunt	Shunt	490	0.065	
Central shunt	No shunt vs. shunt		490	0.52	
Brock's op	No Brock vs. Brock		490	0.52	
VSD size	<20 vs. >20 mm	>20 mm	386	0.45	
Outflow tract patch	**No patch vs. outflow tract patch**	**No patch**	**490**	**<0.001**	**0.008**
Degree of hypothermia	<28° vs. >28°C		459	0.33	
Bypass time	*≤40 vs. >40 min*	*Shorter bypass time*	*484*	*0.023*	
Date of op	**Before 1970 vs. 1970 and after**	**1970 and after**	**490**	**0.026**	**0.010**
Postop RV/LV SBP	≤0.5 vs. >0.5		444	0.73	

*Significant influence on survival is indicated by italic (univariate analysis) or boldface type (multivariate analysis). Abbreviations as in Tables 1 to 3.

years, respectively. No significant differences could be detected between the groups (Fig. 3).

Survival according to previous palliative operations. More than one-third of the patient group (n = 181 [36.9%]) had at least one previous operation (Table 1). The mean age at the time of palliation was 6.0 ± 7.5 years, and the interval to definitive correction was 4.6 ± 2.5 years. Statistics for differences in long-term survival with one and more previous operations or different previous palliative operations (peripheral shunt, central shunt or Brock's operation) were not calculated because of the insufficient number of patients. Although patients with a previous operation had a higher mortality rate during the first postoperative year (80.2% vs. 71.3%, p = 0.013), the long-term outcome in this group was favorable according to univariate analysis, with a 35-year survival rate of 90.1% compared with 83.3% in the nonpalliated group (p = 0.048) (Fig. 4). Multivariate analysis showed no significant influence of a previous palliative procedure on long-term survival because this factor was highly intercorrelated (p < 0.01) with the preoperative hematocrit (HCT) value (see subsequent discussion).

Figure 3. Long-term survival according to patient age at the time of the operation. Long-term survivors were divided into four different age groups. All differences between the groups were not significant. OP = operation.



Survival according to preoperative polycythemia. Patients were divided into two groups according to whether their preoperative HCT level was normal (HCT ≤48%) or not normal (HCT >48%). Patients without preoperative polycythemia had better operative as well as long-term survival (Tables 3 and 4 and Fig. 5). Patients with moderate (HCT between 49% and 59%) and severe (HCT >60%) polycythemia had no differences in their long-term survival.

Survival according to the systolic RV/LV ratio after repair. The results of intraoperative and postoperative measurements of RV and LV pressures were available in 585 patients (88.9%). Patients with an increased RV/LV pressure ratio (>0.5) had a considerably higher mortality risk within the first year (Table 3), independent of transannular patching. However, long-term survival was not affected (Table 4), even if the ratio was substantially increased (>0.7). In fact, patients with an RV/LV ratio >0.7 had a 35-year long-term survival rate of 94.4% compared with 83.7% in patients with a lower ratio. However, this difference was not significant (Fig. 6). Only five long-term survivors with a transannular patch had an RV/LV pressure ratio >0.7. Therefore, the data are insufficient to calculate whether high pressure ratios are less tolerated in the presence of pulmonary valve insufficiency.

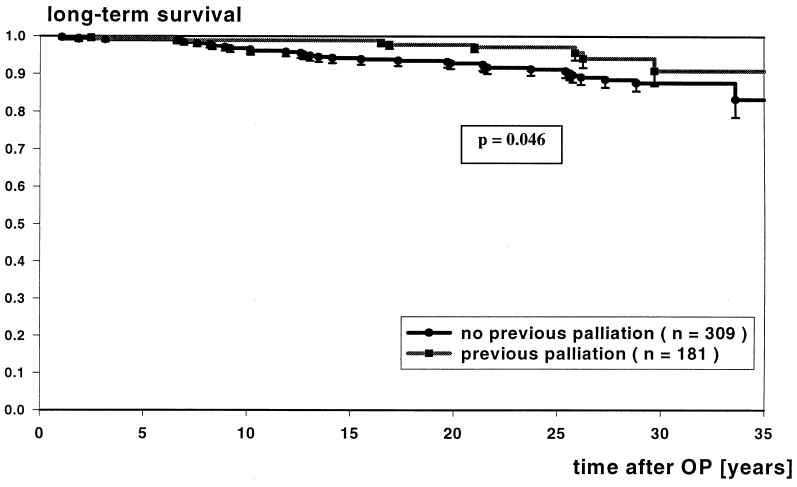


Figure 4. Survival according to previous palliative operations. Long-term survivors with a previous palliative operation showed improved long-term survival. Multivariate analysis demonstrated that this fact was mainly due to the reduction of cyanosis. OP = operation.

Survival according to outflow tract patching. Patients with a need for transannular patching had significantly worse operative and 1-year mortality compared with those with a subvalvular patch or no patch (Table 3). In contrast, long-term survival was impaired by a patch, independent of its location. The 35-year long-term survival rates of patients without a pulmonary outflow tract, those with a patch up to the annulus and those with a patch through the annulus were 86.2%, 79.9% and 78.7%, respectively ($p < 0.05$) (Fig. 7). The presence of an ASD II was significantly associated with the need for an outflow tract patch ($p < 0.01$). Therefore, an ASD II showed adverse effects on long-term survival on univariate analysis. These effects were no longer significant on multivariate analysis.

Survival according to date of operation. To test the hypothesis that the skill of the surgeon affects long-term results, we classified the patients according to the date of their operation. The numbers of patients operated on before 1970 (n = 303) and after 1970 (n = 335) were approximately equal. From a retrospective view, operative techniques and management apparently did not change during the whole period, although minor changes cannot be ruled out. However, operative and 1-year mortality were exactly the same (Table 3), but long-term survival was significantly improved for patients operated on during the latter period (Fig. 8).

Survival with diagnosis of "low risk" TOF. Because preoperative polycythemia and the need for outflow tract patching were the only significant patient-related factors on multivariate analysis, the survival of patients without preoperative polycythemia and no need for outflow tract enlargement (n = 169) was compared with that of the normal population. No difference in 35-year long-term survival could be detected (Fig. 9).

Follow-up data. More than 90% of the patients reported themselves to be in New York Heart Association functional class I or II at the time of follow-up, 96.5% of whom were in a better condition than that before the operation. Most patients were in the workforce (70.8%) or housewives (20.1%); only 6.1% had retired and 3% were unable to work. However, 32.3% of the patients (n = 137) reported cardiac symptoms, mainly signs of congestive heart failure as dyspnea (n = 119

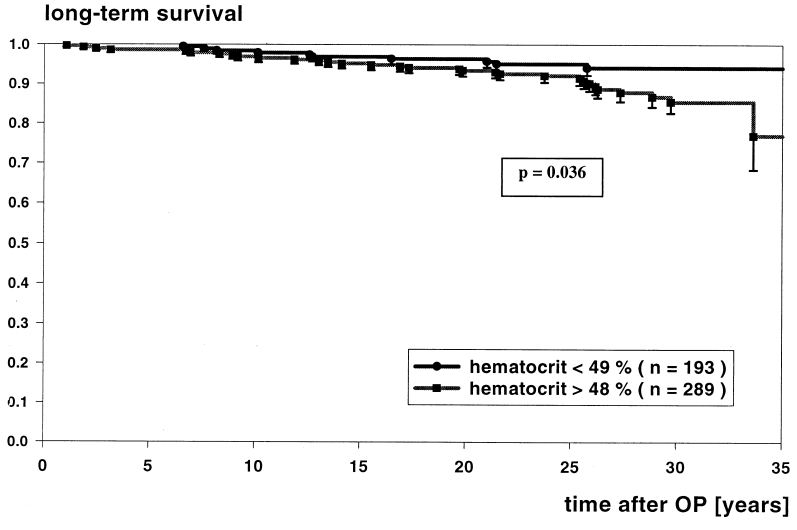


Figure 5. Long-term survival according to preoperative polycythemia. Patients with normal HCT levels (≤48%) showed improved long-term survival on univariate and multivariate analyses. OP = operation.

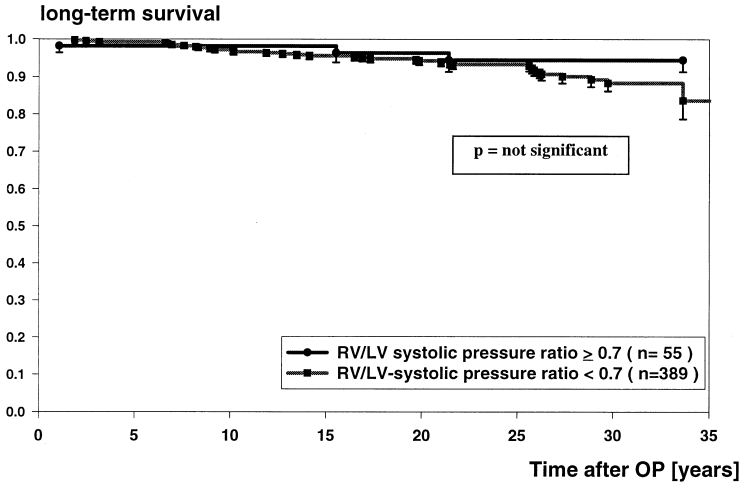


Figure 6. Long-term survival according to the postoperative systolic RV/LV pressure ratio. The RV/LV pressure ratio showed no influence on long-term survival even if it was severely increased (RV/LV ≥0.7). OP = operation.

[26.7%]) or edema (n = 39 [8.8%]). Arrhythmias were also commonly reported (n = 60 [14.2%]). Myocardial infarction occurred in three patients (0.6%) and one (0.2%) had angina pectoris. Five patients (1.2%) developed endocarditis and six (1.4%) had hepatitis. A new heart catheterization was performed in 140 patients (32.9%) and 106 (25%) were taking medication.

Reoperations with ECC. During the first year, five patients, and during subsequent long-term follow-up another 31 patients, had a second operation with ECC, resulting in freedom from reoperation of 91.8% after 35 years (Fig. 10). The most common cause of reoperation was a residual or reopened ventricular septal defect in 29 patients, followed by a combined VSD with outflow tract restenosis in three patients and sole restenosis in four patients.

Heart rhythm and implantation of pacemakers. On the electrocardiogram at discharge, 26 patients (5.3%) had an atrioventricular (AV) block I, 4 patients had an AV block II (0.8%) and 3 had an AV block III (0.6%). A pacemaker was implanted in the immediate postoperative course in 11 patients with AV block (2.2%). During the follow-up period, another four patients received a pacemaker.

Discussion

The excellent long-term survival after correction of TOF, even in the very early years of cardiac surgery, is well recognized (4). However, it remains uncertain whether the results last longer than 25 years. It has been speculated that RV failure might occur late after correction (6) and the incidence of sudden cardiac death, the most common cause of late death (7), might decrease if patients survive into adulthood (8,9). Our results show a significant impairment of survival >25 years postoperatively, and sudden cardiac death remained the major cause of death in these adult patients. This was not true for patients without the need for an outflow tract patch and normal preoperative HCT levels; they achieved normal life expectancy up to 35 years postoperatively.

Sudden cardiac death during long-term survival. Sudden cardiac death is mainly attributed to ventricular dysrhythmias

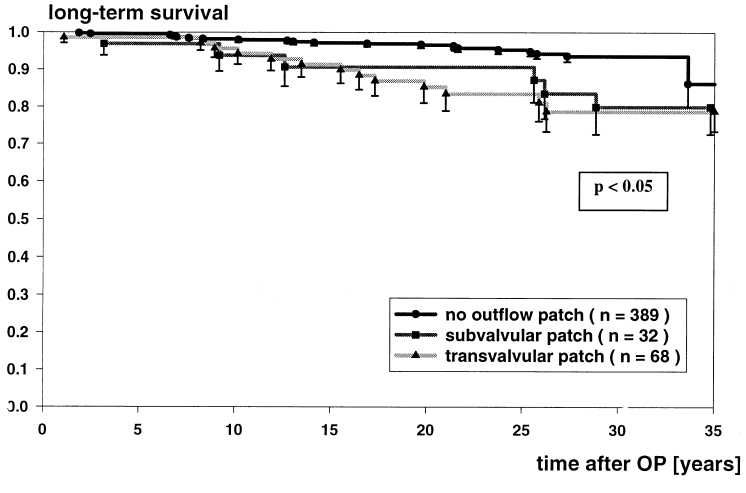


Figure 7. Long-term survival according to an RV outflow tract patch. In the majority of patients no outflow tract patch was necessary. If the ring of the pulmonary valve was severely hypoplastic, a patch through the annulus was used to widen the outflow tract. In some patients, a patch up to the annulus but not through it seemed sufficient to relieve obstruction. OP = operation.

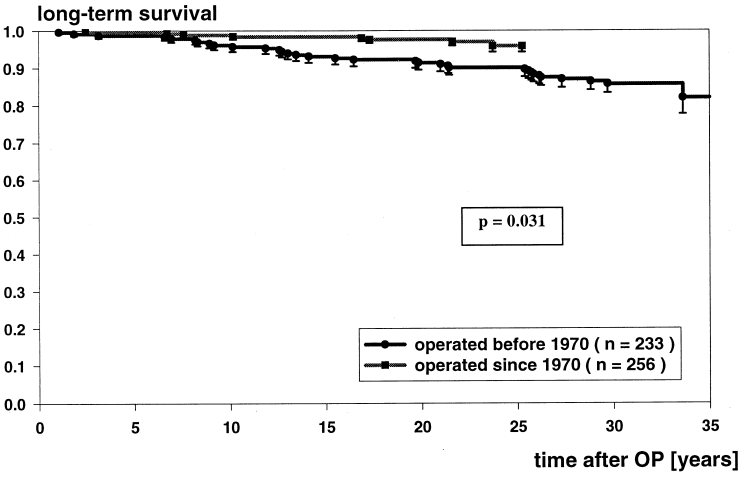


Figure 8. Long-term survival according to the date of the operation. Throughout the whole period, operative management and techniques did not change. However, patients operated on after 1970 showed improved long-term survival. This has to be attributed to the growing experience of the single surgeon. OP = operation.

(10); other less common causes are complete heart block (11) or sick sinus syndrome. Chronic RV overload due to pulmonary regurgitation is related to diastolic function and correlates with QRS prolongation, which is the most sensitive predictor of ventricular arrhythmias (12). Therefore, chronic pulmonary regurgitation caused by a valveless outflow tract patch may lead to progressive RV enlargement and sudden cardiac death. Studies in patients with congenital isolated pulmonary regurgitation showed that the RV fails after 40 years of successful adaptation (13).

Impact of an outflow tract patch on long-term survival. The influence of an outflow tract patch on long-term survival is controversial. Kirklin et al. (14), as well as Murphy et al. (4), could not find any differences in long-term survival between patients with and without an outflow tract patch. Jonsson and Ivert (15) and our earlier follow-up data (16) showed contradictory results. In our patients, use of an outflow tract patch remains to be the most important risk factor for late death. The average age in the studies of Kirklin (median 5.3 years) and Murphy (mean 10 years) tends to be lower than that in the study of Jonsson (median 7 years) and also lower than that in our study (mean 12.2 years, median 9.2). The same is true for the preoperative HCT level (see below). This indicates that in time, the RV might stiffen due to increasing hypertrophy and becomes less capable of adapting to pulmonary insufficiency. Another possible explanation for our finding could be the change in operative approach from a horizontal to a vertical ventriculotomy whenever an outflow patch was deemed necessary. It has been shown that the technique of cardiotomy significantly effects RV enlargements and consequent arrhythmias (17).

Impact of the RV/LV pressure ratio on long-term survival. Avoidance of an outflow tract patch would lead to the acceptance of higher postoperative systolic RV/LV pressure ratios. Increased RV/LV pressure ratios after corrections are clearly a risk factor for operative death, but the influence on long-term survival remains as controversial as the outflow tract patch. In contrast to the studies by Kirklin and Murphy, both Jonsson's study and our study could not show any influence of a high pressure ratio on long-term survival. It might be explained by a similar hypothesis that older, more hypertrophied hearts could better tolerate a persistent pressure load.

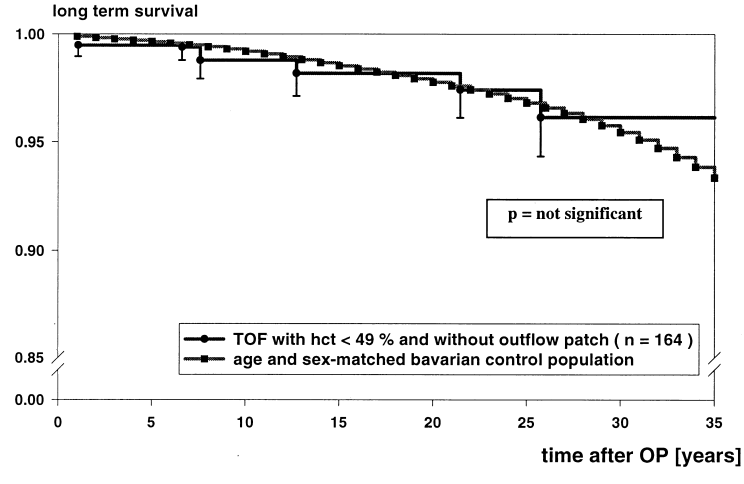


Figure 9. Normal life expectancy in a subgroup of patients. On multivariate analysis, only use of an outflow tract patch and preoperative polycythemia were patient-dependent risk factors. A comparison between a low risk group of patients (no outflow tract patch and no preoperative polycythemia) and an age- and gender-matched control group of the Bavarian population shows no difference in long-term survival up to 35 years. Thus, subgroups may achieve normal life expectancy. OP = operation.

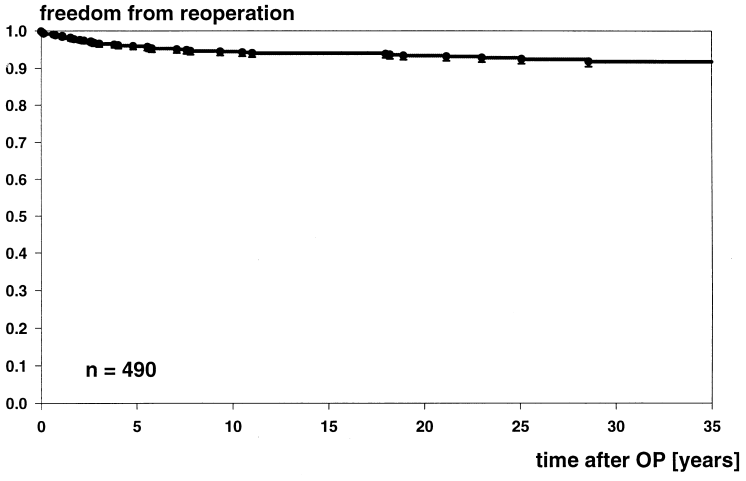


Figure 10. Occurrence of reoperations in long-term survivors. Reoperations were performed in 42 long-term survivors during follow-up. OP = operation.

Impact of age on long-term survival. In contrast to most other studies, older age was not associated with an increased mortality risk. A striking explanation for this fact is lacking. The number of older patients in our study is higher (Fig. 3) than that in all other studies where age was found to be a risk factor; completeness and length of follow-up add to the statistical power of our analysis. The Mayo Clinic reported on 30 patients who had corrections at the age of ≥40 years (18). Long-term survival was not different from that in a normal age-matched control population, but was higher than that for medically treated patients.

Impact of other risk factors on long-term survival. Multivariate analysis demonstrated increased HCT levels as an additional risk. Data on preoperative polycythemia as an incremental risk factor is disagreeing. Zhao et al. (19) could not find any association between HCT and outcome, whereas Kirklin et al. (20) shared our experience. However, the mean HCT values in our study are higher than those reported by Kirklin and Zhao (54% vs. 49%), which may in part explain the differences.

Surgical experience has been identified as a risk factor for operative mortality (21), but to the best of our knowledge, it has never been tested as a risk factor for long-term survival. In our patient group, it seems to be a strong predictor of late death, although it cannot be excluded that perioperative management improved in parallel with surgical skill and added to better long-term outcome. However, this result further encourages repair of complex congenital heart defects only by experienced surgeons in high volume centers. Other postoperative factors such as ventricular function, arrhythmias and pulmonary insufficiency are likely to influence long-term survival in this patient group (6,9,12). Because of the retrospective nature of this study, data on these important issues were not available.

Interpretation of operative and 1-year survival. Indication, surgical technique and operative mortality of the correction of TOF have changed dramatically since the early days of cardiac surgery (22–24). Operations were performed in older children, and only insufficient cardioprotective measures were used. The combination of TOF with other major heart malformations, previous shunt operations and any other reason to prolong ischemic arrest, leads to a significant increase in mortality rates. Therefore, interpretation of risk factors for short-term survival in this historic experience is of very limited value to contemporary practice. However, the isolation of a PFO as a beneficial factor in multivariate analysis encourages the widely used practice of leaving it open during repair to allow right to left decompression in case of postoperative, temporary RV failure (25).

Coping with TOF. Suicide is a common cause of late death reported in almost all of the large series. Lillehei et al. (1) and Rosenthal et al. (26) attributed 10% of late deaths to suicide. In our own study, two patients committed suicide and in two other patients suicide was likely but not confirmed; their deaths were classified as unknown cause. This high incidence of suicide might be the most striking evidence that, after successful repair, patients often have psychological problems such as low self esteem, lack of confidence and concern about performing physical activity (27,28). Baer et al. (29) demonstrated that neurotic behavior can be avoided by repair early in childhood. Psychological support should be considered as one important aspect in long-term care.

Conclusions. Our results demonstrate that in older children with very hypertrophied RVs, the most important factors for long-term survival are avoidance of polycythemia and a RV outflow patch, as well as an experienced surgeon. Adding data from other studies of younger patients, repair early in life may avoid some of the risks the older patients have to face. Despite the fact that some patient subgroups may achieve normal life expectancy, TOF remains a life-long disease that is not cured by repair.

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