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Single-center 50 years' experience with surgical management of tetralogy of Fallot☆

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Abstract

Objective: The aim of this study was to evaluate the long-term outcome of total repair for tetralogy of Fallot. We aimed to characterize late survival and the time-related risk of late reoperation. **Methods:** Operative protocols, patient records, and the database of the department were evaluated from 1951 until 2008. The official death registry of Norway was used for follow-up. Of the patients identified, the follow-up was 99.6% complete. **Results:** A total of 627 patients were studied. Of these, 570 could be identified for follow-up. There were a total of 41 early and 30 late deaths. The total early (including palliative procedures) mortality was 7.2% and total late mortality was 7.9%. However, during the last 10 years, no early mortality has been observed following repair. A total of 264 patients underwent some form of palliative procedure as their first treatment, and 541 patients had a reparative procedure performed, with an early mortality of 31 (5.7%). In patients subjected to a reparative procedure, there was no difference in freedom from death or reoperation following primary repair versus primary palliation. The use of transannular patch was associated with a highly significant risk of reoperation. **Conclusions:** Surgical treatment of the tetralogy of Fallot and related congenital cardiac malformations has good long-term prognosis. In this cohort of patients, more than one-third required additional procedures later on, and, in some cases, as many as four additional surgeries. Palliative procedures followed by repair do not influence survival or reoperation-free survival. There are no differences between transatrial versus transventricular repair on survival or re-repair. Any transannular incision increases the risk of re-repair, but does not influence long-time survival. There is an almost linear decrease in reoperation-free survival following any type of repair of tetralogy of Fallot, even for as long as 50 years since the first procedure.

Keywords: Congenital heart disease; Tetralogy of Fallot; Pulmonary insufficiency

1. Introduction

Surgical correction of tetralogy of Fallot (TOF) was initiated by Lillehei in 1954 using controlled cross-circulation in a 10-year-old boy [1]. Since then, this most common cyanotic heart disease has been extensively studied and there still exist controversies whether early primary repair or a two-stage approach is the technique of choice [2]. Early primary repair is preferred for several reasons, including reduction of right ventricular pressure overload and elimination of hypoxemia and cyanosis and secondary organ damage. The trend is to correct Fallot in infancy even if this might imply a more frequent use of transannular patch (TAP). A recent study spanning four decades claimed that the nature of the original corrective procedure did not influence either late risk of death or risk of PVR [3]. However, different indications and timing of redo procedures exist and this will affect the incidence of reoperations. The growing population of adults presently living with repaired TOF represents an excellent substrate for evaluating the time-related risk of death, reoperations, and pulmonary valve replacement. We report our surgical experience spanning five decades with surgical treatment of TOF.

2. Material and methods

The hospital's database and all medical records and operation room protocols of all patients who underwent operation for TOF at Rikshospitalet between 1 January 1952 and 31 December 2008 were included in the study. TOF was diagnosed using established morphological criteria and the material also included those operated for double-outlet right ventricle (DORV) type of TOF, pulmonary atresia (PA) of TOF type, including AV-canal with or without Down's syndrome and absent pulmonary valve. During the early days of cardiac surgery and until 1971, the patients were registered with their name as the only ID, without giving the age or day of birth. The official death registry of Norway is incapable of identifying persons by name only. This registry, which

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registers persons alive or dead, was used for follow-up. Out of 627 patients, 570 could be identified for follow-up in this registry, and is included in the study group. A total of 306 patients had primary repair of TOF without any prior palliative procedure and 264 patients had a primary palliative procedure. Of these, 29 patients have undergone a palliative procedure only, leaving a total of 541 repaired patients. Hospital records from Rikshospitalet, including earlier surgery, were used for classification of procedures performed. Procedures at an elsewhere hospital during the study period was included in the study. One patient had moved abroad during the study period and this patient was lost to late follow-up.

Classification of repairs: (1) Transatrial approach, with or without PA patch. (2) Transventricular repair, with or without infundibular or PA patch. (3) Transventricular approach with TAP. (4) Same as above, with monocusp in PA. (5) Repair with conduit or valve insertion: Biological valves include Carpentier Edwards, Hancock, Perimount, Cryopreserved allografts, Homologous tissue, Mechanical valves include Carbomedics, Medtronic Hall, On-X, St. Jude, Other valves: Goretex bicuspid. Conduits used were: Cry preserved allograft, Contegra bovine jugular, Shellhigh, Polystan bovine jugular, Ionescu-Shiley, Hancock, Goretex mono/bicuspid. The variety of different prosthetic materials used during this long-time span caused relatively small numbers in each group not qualifying for statistical analysis between these groups.

2.1. Statistical analysis

Categorical variables were compared using chi-square test and continuous variables were analyzed using the Wilcoxon rank-sum method or Students unpaired *t*-test. Early mortality was defined as death within 30 days of operation. Kaplan–Meier method was used to analyze long-term survival and freedom from reoperation. Differences between survival distributions were assessed by log-rank testing. Probability values less than 0.05 were considered significant for all tests.

3. Results

Operative data, such as bypass-times, cross-clamp time, and need for IPPV, were not available for the data collected before 1999, and could not be reported. The use of TAP and other types of repair could be retrieved from operating room protocols. Operative data showing the type of repair in the different time periods are shown in Table 1.

The total early (including palliative procedures) mortality was 7.2% and total late mortality was 7.9%. However, during the last 10 years, no early mortality has been observed following repair. The numbers, early mortality, late mortality, and time interval of the different types of repaired patients are shown in Tables 1 and 2.

The age at repair has been reduced. Still, we do a primary repair (using transannular approach in 50%) in only 60% of our patients as shown in Tables 1–4.

The follow-up period spans nearly six decades, and 56 patients were lost to follow-up because of lack of identification in the early period. One patient was lost because of moving abroad during the late period. The median follow-up time was 15.8 years. Fig. 1 demonstrates the type of repair during different time periods and illustrates the change in strategy. A tendency toward primary repair was registered.

The significance of primary repair versus primary palliation was also analyzed. In the patients who underwent a reparative procedure, there were no differences in freedom from death or reoperation in the 50-year period, as displayed in Fig. 2.

Table 1. Different types of repair during the decades.

Type of repair	Decades					
	1	2	3	4	5	Total
1	0	1	2	19	53	75
2	21	90	90	53	26	280
3	0	5	6	9	8	28
4	0	0	5	50	47	102
5	1	6	9	14	26	56
Total	22	102	112	145	160	541

Types of repair: 1 = transatrial; 2 = transventricular; 3 = transventricular with transannular patch; 4 = transventricular with transannular patch and monocuspid valve; and 5 = valve or conduit in right ventricular outflow tract. Decades: 1 = before 1971; 2 = 1971 through 1979; 3 = 1980 through 1989; 4 = 1990 through 1999; and 5 = 2000 through 2008.

Table 2. Mortality following different types of repair.

Type of repair	Number	EM	%EM	LM	%LM	TM	%TM
1 (transatrial)	75	0	0	2	2.7	2	2.7
2 (transventricular)	280	27	9.6	19	6.8	46	16.4
3 (TAP)	28	0	0	2	7.1	2	7.1
4 (TAP + MC)	102	2	2	1	1	3	3
5 (conduit/valve)	56	2	3.6	6	10.9	8	12.7
Total	541	31	5.73	30	5.55	61	11.28

EM: early mortality; LM: late mortality; TM: total mortality; TAP: transannular patch; and MC: monocusp valve.

Table 3. Age at surgery and intervals.

	Number	Median age at first operation (days)	EM (%)	Median age at repair (years)	EM (%)	Interval between palliation and repair (years)
Primary repair	306			1.90	21 (6.9)	
Primary palliation	235	144		2.92	10 (4.3)	1.88
Palliation only	29	71	10 (34)		20 (8.5)	
Total	570			2.33	41 (7.2)	

Table 4. Early mortality (EM) during different decades and different approaches.

Decades	Total	Age at repair	% Primary repair	R-P+R-P	EM (R-P+R-P)	%EM
1. 1953–1971	22	15.34	48.0	12-13-3	9 (6-2-1)	40.1
2. 1971–1979	102	6.05	64.0	71-34-6	16 (8-5-3)	15.7
3. 1980–1989	112	2.99	48.3	58-58-4	12 (6-2-4)	10.7
4. 1990–1999	145	2.02	46.4	71-74-8	3 (1-1-1)	2.1
5. 2000–2008	160	1.02	58.4	94-66-1	1 (0-0-1)	0.6

P: Primary repair; P+R: palliation before repair; and P: palliation only.

We had 32 complicated cases including PA, absent pulmonary valve syndrome, and A-V canal. Out of these, absent pulmonary valve syndrome accounted for 16 cases alone. We were not able to show any statistical worse outcome for these patients.

The freedom from reoperation, following the use of a transannular involvement or not was analyzed, and is displayed in Fig. 3. This diagram clearly illustrates the fact that a highly significant difference was noted between the groups. However, note that the difference becomes clear only after more than 10 years of observation.

We looked carefully on the results expressed as survival and freedom from reoperations during different time periods. The time frame (50 years) was analyzed divided into five decades and as Fig. 4a and b shows we were not able to show any statistically different long-term results. However, the early mortality was significantly higher during the first decade. This is clearly expressed in Fig. 4.

4. Comment

Several controversies exist concerning the optimal treatment of TOF: the timing and character of initial surgery, when to intervene for secondary pulmonary insufficiency, and what kind of prosthesis to use in the RVOT. Primary repair during infancy may need more frequent use of TAP but the association between the use of TAP and long-term outcome is uncertain [4]. However, the present study, to our knowledge the study with the longest follow-up time to date, demonstrates that TAP significantly increases the need of redo procedures.

Several studies have demonstrated that correction of Fallot may be performed safely in infancy [5,6]. Recent studies advocate early repair based on excellent follow-up figures. However, late outcome is still uncertain as most follow-up periods have only been for a limited period of time [4–6]. We are able to show a significant difference in long-term outcome. TAP is strongly associated with later redo

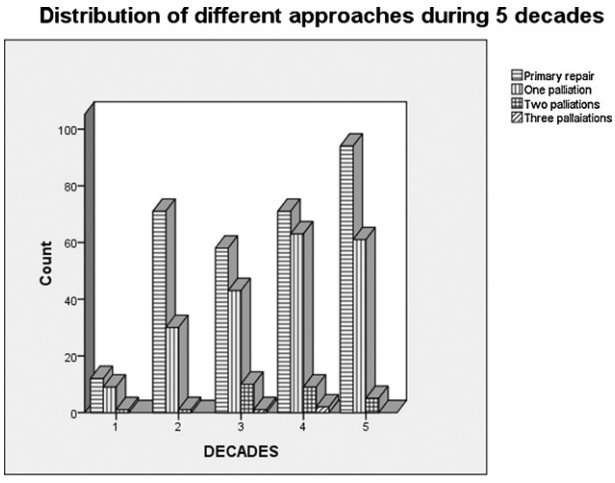

Fig. 1. Distribution of different type of approaches during the five decades, with patients primary repaired or undergoing a different number of palliation before repair.

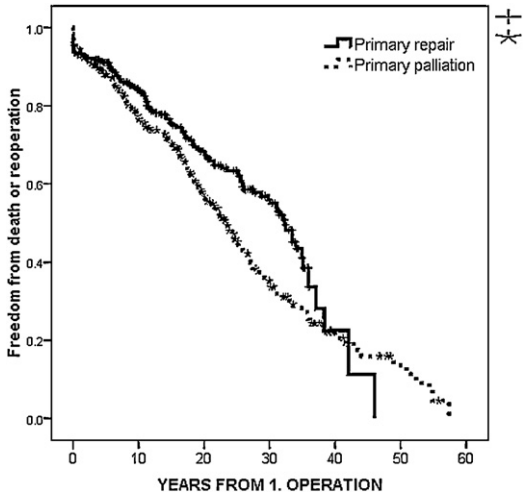

Fig. 2. Long-time follow-up after different approaches in surgical treatment, primary repair or primary palliative surgery.

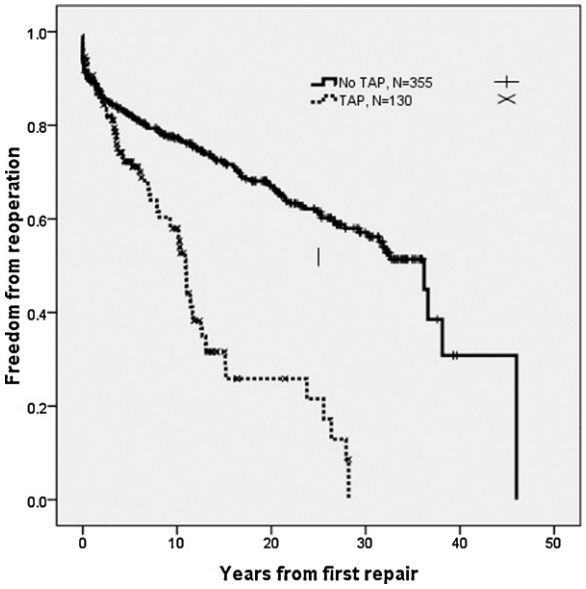

Fig. 3. The influence of repair crossing the pulmonary annulus upon freedom from reoperation following surgery for tetralogy of Fallot.

procedures. We know from several studies that correction in infancy carries a higher risk of TAP [5]. Whether this observation is a reflection of the morphology and severity of the original condition or age at repair is difficult to say. We hypothesize that most institutions, like ourselves, correct the anatomical favorable patients while palliating the others. This confounding factor may attribute to different results.

Tamesberger recently stated that several authors including their own group reported that the use of TAP did not reduce late survival and was associated with a lower incidence of RV tract obstruction [6]. Their median follow-up time was 4.7 years and at that time point their findings were in accordance with our registration. However, from 10 years on we can clearly demonstrate that a significant worse outcome is registered in the TAP group. d'Udekem et al. also reported in *Circulation* that TAP and RV patching equally affect late functional status [7]. We propose, based on our present data, that conclusions based on a limited follow-up time must be interpreted very cautiously.

Children with TOF usually have a higher rate of extracardiac anomalies and syndromes [8], which are thought to further increase the risk of open heart surgery especially in the neonates. Premature infants and neonates, especially those with severe cyanosis or duct-dependent pulmonary circulation, represent a group of patients for whom open heart surgery is frequently postponed in favor of palliative procedures that can be carried out without cardiopulmonary bypass. It has been shown that infants less than 3 months of age have a higher morbidity rate compared with older infants and had a more frequent need for peritoneal drainage, a longer time to extubation, and longer stay in the intensive care unit [2]. Reports of TOF repair since 1992 have shown that younger age and TAP are associated with increased risk [1,9]. Some previous studies have also shown that age at operation less than about 6 months, low weight, and TAP reconstruction of the RVOT are all associated

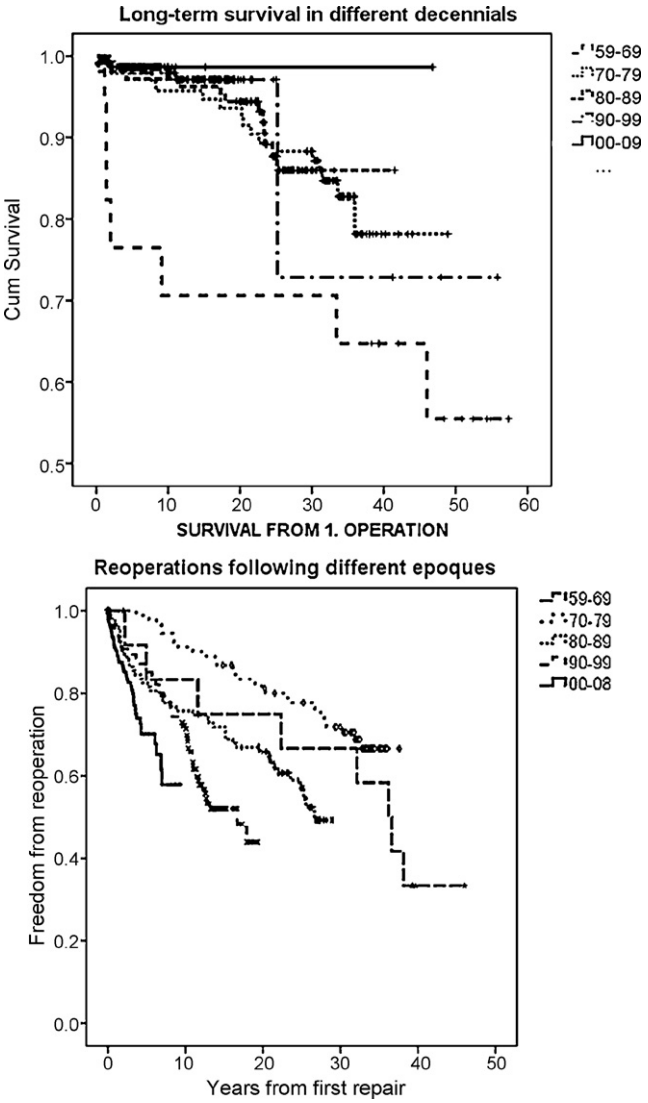

Fig. 4. (a, b) Survival and frequency of reoperations during the five different decennials following surgery for tetralogy of Fallot.

with increased mortality after intracardiac repair. However, recent reports document current safety of repair within the first year of life [10]; hence, controversy exists about the optimal timing and choice of procedure.

Optimal timing of PVR has yet to be determined. PVR through eliminating pulmonary regurgitation improves functional status. It has been shown that PVR is important in RV remodeling and stabilizes QRS duration [11]. Some advocate early PVR to avoid onset of dangerous arrhythmias [12]. The ideal prosthesis has yet to be found and in our institution several biological alternatives, mechanical prosthesis, autologous valve creation, and customized Gore Tex valves have been used. Our present policy is to be aggressive in replacing insufficient and/or stenotic valves or prosthesis. The risk associated with a redo procedure in the present era is very low, and the risk associated with severe volume overload is significant. Presently, we predominantly use biological stented prosthesis, although some autologous created valves are being used.

5. Conclusion

Surgical treatment of TOF can be done safely both as a primary repair and as a staged procedure with very low mortally and morbidity during infancy. Surgical correction as the primary procedure is today the most preferred intervention; however, it may carry a higher risk of TAP in early age than the sequential technique. Long-term follow-up reveals that patients subjected to TAP exhibit a significant higher risk of redo procedures. It, therefore, seems wise to carefully select patients for primary repair in early infancy, where preservation of the pulmonary annulus seems possible.

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Appendix A. Conference discussion

Dr R. Prêtre (*Zurich, Switzerland*): Dr Lindberg and the Oslo group report their whole experience with the treatment of Fallot's tetralogy. It spans 50 years as the title says even though the mean follow-up, a remarkable follow-up by the way, is 'only 16 years.' This analysis is another step forward, but still I think not the end of the story of the Fallot patients. And your conclusions, although very strong, are probably not definitive.

This is a remarkable study not only from the epidemiological, but also from the surgical point of view, and it has confirmed, more or less, what we have already lately established, that is, that life expectancy and quality of life after Fallot repair are very good, but at the expense of many reoperations or reinterventions.

My questions now. You showed that the use of primary palliation had no influence on mortality or even on freedom from reoperation. Has this finding, or will this finding influence the way you treat Fallot? In other words, what are or what will be your indications for palliation in those patients?

My second question, we were expecting problems on the right ventricular outflow tract, and this came 10 to 20 years after the repair. We can also foresee a problem on the left side of the heart because many patients have some significant aortic valve insufficiency or dilatation of the ascending aorta.

Have you seen this problem coming up in your longest follow-up patients?

Dr Lindberg: About the indications, from the conclusions of this study we believe that any incision of the pulmonary annulus should be avoided. So we do a repair if we think that the pulmonary annulus can be preserved if it is a newborn, or whenever it presents with the indications for treatment. And if there is a pulmonary annulus insufficient for what we think is an acceptable gradient postoperatively, we do a palliation.

On the left-sided problems, yes, we have seen that. I think as a first reoperation, an aortic intervention was necessary in three patients. But it also happened in, I believe, three patients in combination with the right ventricular outflow tract repair. And in those three patients, I do not think that the aorta would have been touched by itself because this was a very mild insufficiency, but there was some dilatation of the ascending aorta. So we put in an ascending graft to prevent any further dilatation.

And later on there have been many — I think it was about one for every reoperation, one for the third, one for the fourth, and even one for the fifth reoperation, there was one that included the aorta.

So grand total, I think it is about 10 aortic reinterventions from this patient group, which is not a very high number.