Follow-up in the Surgical Treatment of Tetralogy of Fallot

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Objective: The purpose of this study is to evaluate the early and intermediate results after total correction of Tetralogy of Fallot in 193 consecutive patients, with a mean age of 29 months, who underwent surgical correction in Transplant and Cardiovascular Disease Institute Târgu Mureş between 2005 and 2011.
Methods: The records of these patients were reviewed. Follow-up was obtained through clinical appointments and telephone questionnaires.
Results: One-hundred forty-four (74%) patients underwent single-stage complete repairs; 49 (25%) patients underwent initial palliative operations (systemic-pulmonary shunt), whereas 40 (20%) of them underwent secondary total corrections. Early and late mortality was 2% (n=4) and 2.5% (n=5), respectively. Mean follow-up was 35 months (range: 4 months to 71 months). Respiratory infection was a risk factor for early mortality (p=0.0032). For the reconstruction of the right ventricular outflow tract we used 21 valved conduits, 68 transannular patches and for the others patients right ventricular patches + pulmonary valvuloplasty/valvulotomy. On late postoperative echocardiography, 59 patients presented moderate pulmonary regurgitation, 21 a small residual ventricular septal defect, 4 severe residual dynamic stenosis of RVOT and 5 calcifications of the transannular patch, for whom we carried out 7 replacements of the pulmonary valve and 14 reconstructions of the right ventricular outflow tract.
Conclusions: Surgical repair of patients with simple or complex forms of tetralogy of Fallot can be achieved with low early mortality. Late mortality and the need for reoperation continue to influence the quality of life for these patients.

Keywords: Tetralogy of Fallot, congenital, obstruction, pediatric surgery

Introduction

Tetralogy of Fallot is the 5th most frequent cardiac malformation, representing approximately 6.8% of the total of congenital cardiac malformations. Its incidence is 0.19–0.26/1000 live births, being the most frequent cyanotic congenital cardiac malformation encountered after the age of one week. Family recurrence is 1.5% for fathers and 2.5–4% for mothers with Tetralogy of Fallot; in case of deletion of the 22q11 chromosome, the risk of recurrence is 50% [1].

From an anatomical point of view, this cardiac malformation consists of four fundamental abnormalities: pulmonary infundibular stenosis, ventricular septal defect, overriding aorta and right ventricular hypertrophy. There is a great variability of these abnormalities, concerning the anatomy of the ventricular septal defect, the nature and degree of pulmonary infundibular stenosis and the degree of dextroposition of the aorta [1].

From an etiological point of view, this pathology can be explained through the prism of embriology. The antero-cephalic deviation of the infundibular septum, with its fibrous persistence, associated with the hypertrophy of the septoparietal trabecula will result in the obstruction of the ejection tract of the right ventricle, a characteristic abnormality for the Tetralogy of Fallot. Also, this deviation is responsible for the misalignment and defect of the ventricular septum, leading also to the dextroposition of the aorta. The hemodynamic consequence of these anatomical modifications is right ventricular myocardial hypertrophy [2].

The high number of cases of Tetralogy of Fallot in the casuistry of the Institute of Cardiovascular Diseases and Transplant of Târgu Mureş determined us to carry out a retrospective observational study, which included the perioperative and postoperative short- and mid-term follow-up of patients, in order to highlight surgical performance parameters (survival rate, reintervention rate), pre- and postoperative care parameters, to identify certain risk factors and to compare the results with those obtained in other centers of pediatric cardiac surgery.

Material and methods

We included in the study 193 patients with Tetralogy of Fallot, who underwent a surgical intervention between October 2005 and August 2011, in the Institute for Cardiovascular Diseases and Transplant and the Center for Cardiovascular Diseases and Transplant of the County Emergency Clinical Hospital of Târgu Mureş. The patients were aged between 1 week and 16 years. The observation charts of these patients were analyzed in a proportion of 100%. The length of follow-up was 35 months in average (between 4 and 71 months) and was carried out through periodic consultations and telephone questionnaires. Long-term follow-up rate was 92% due to the loss of data for 15 patients, but their latest data showed a favorable evolution. The data was centralized in Microsoft Excel and statistical analysis was carried out with SPSS v. 19 for Windows (Statistical Package for the Social Sciences, Chicago, Illinois). We used Kaplan-Meier survival curves and Fisher's test.

Table I. Morphological data

Morphological data	No. (%)
Pulmonary truncus and branches	
Atresia	13 (6.73%)
Hypoplasia	59 (30.56%)
Normal	2 (1.03%)
Pulmonary valve	
Atretic	17 (8.8%)
Dysfunctional	63 (32.64%)
Interatrial communication	
Ostium secundum ASD	24 (12.4%)
Patent Foramen Ovale	31 (16.06%)
Patent Ductus Arteriosus	49 (25.38%)
Coronary anomalies	4 (2.07%)
Ventricular septal defect	
Single	190 (98.44%)
Multiple	3 (1.55%)

Results

Preoperative data

There were 104 boys (53.8%) and 89 girls (46.2%) included in the study. We had 10 patients aged under 1 month, 57 patients between 1 month and 1 year (29.5%), 76 patients between 1 and 3 years (39.3%), 25 patients between 3 and 6 years (12.9%) and 25 patients above 6 years (12.9%). The average age was 37 months, with a tendency to decrease in the last two years. The modifications of cardiac morphology and their manifestations, e.g. the varying degree of obstruction of the right ventricular outflow tract (RVOT), the presence of pulmonary hypoplasia or atresia or the presence of other competent blood sources towards the pulmonary circulation, enable the discovery of this pathology at birth or even during pregnancy and determine the type of surgical intervention to be performed. On the contrary, the lack of symptoms may delay the diagnosis to advanced ages (Table I). Pulmonary atresia was present in 13 patients, in whom the presence of patent ductus arteriosus or aortopulmonary collaterals is of vital importance. The obstruction of the RVOT was present in its most common form at infundibular level (in 45% of cases) and only rarely at pulmonary level (in 10% of cases). A combination of these lesions was present in 30% of cases. The pulmonary valve was atretic in the most severe form of this malformation (in 9.5% of cases). The pulmonary ring and the truncus of the pulmonary artery were hypoplastic in the majority of patients.

Table II. Postoperative complications in the ICU

Postoperative complications in the ICU	No. of patients
Infectious	
Sepsis	7
Bronchopneumonia	44
Urinary tract infections	5
Cardiac	
Arrhythmias	31
Heart failure	36
Hematological	
Hemorrhage	4
Thrombopenia	11
Kidney failure	9
Liver failure	4
Respiratory	
Severe tracheal stenosis	5
Edema of glottis	4
Pleurisy	9
Neurological	
Hypoxic encephalopathy	5
Convulsions	8
Motor agitation	5
Hemorrhagic stroke	1
Deaths	4

Coronary artery abnormalities were present in 4 children. Of these, we most frequently encountered the anterior descending artery originating from the right coronary artery, descending over the outflow tract of the right ventricle. This coronary abnormality may impose a different surgical approach in the case of transanular ventriculotomy, becase there is a risk to damage the anterior descending artery. Seven patients needed preoperative mechanical ventilation, 12 patients needed the administration of prostaglandins and 5 patients needed inotropic support.

Surgical data

We carried out a total primary correction for 144 of the 193 patients (74.6%). We used 21 right ventricle-pulmonary artery valved conduits (16 of which were made by the research team of our clinic and 5 were Contegra valved conduits), 68 transannular patches (5 unvalved and 63 valved), while in the rest of the patients we used outflow tract enlargement patches accompanied by pulmonary valvuloplasty/valvulotomy. Infundibular muscle resection was performed in 95% of patients, sometimes being enough to eliberate the RVOT. In the other 49 patients, where the

Table III. Late postoperative complications and the type of reinterventions

Late complications	No.	Reinterventions	No.
Severe/moderate pulmonary regurgitation	4/55	Replacement of the pulmonary valve	7
Residual ventricular septal defect	21	Closure of the residual ventricular septal defect	4
Tricuspidal regurgitation	23	Tricuspidal annuloplasty	14
Residual dynamic stenosis of the RVOT	4	Reconstruction of the RVOT	5
Calcification of the transannular patch	5	Replacement of the transannular patch	5
Obstruction of the RV-PA valved conduit	5	Replacement of the RV-PA valved conduit	5

Table IV. Meta-analysis

	Our study	Study A [4]	Study B [5]	Study C [6]	Study D [7]	Study E [8]
Early mortality (<30 days)	**2%**	0.6%	4.5%	0%	6.9%	3.7%
Survival at 6 years	**90%**	93%	92%	93%	91%	94.8%
Average follow-up (months)	**32**	62	60	24	34	150

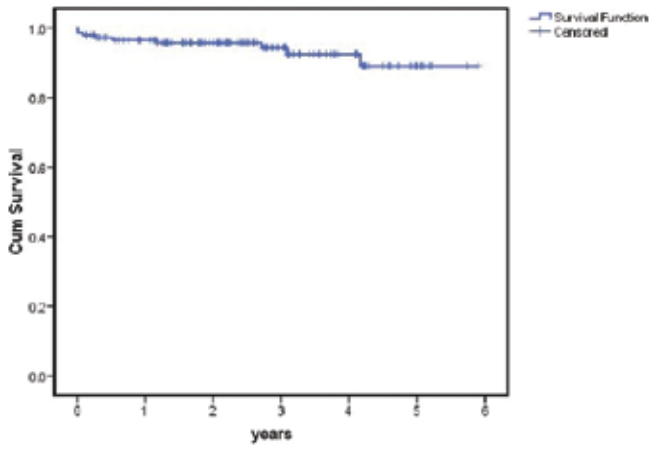

Fig. 1. Kaplan-Meier curve

pulmonary truncus and branches were able to sustain a minimal blood flow, we opted for palliative surgery, performing a Blalock-Taussing systemic-pulmonary shunt (15 central and 34 peripheric). Of these patients, after an average period of 13 months (range 8-16 months), during which the favorable conditions for a secondary total correction were created, 40 patients benefitted from this treatment. The average duration of cardiopulmonary bypass was 104.3±30 minutes, and aortic clampage took 68±16 minutes. There were no intraoperative deaths recorded.

Postoperative data

Prognosis depends on the postoperative evolution of the patients in the Intensive Care Unit, and their care requires meticulosity, increased attention and performing equipment. Nevertheless, complications are inevitable, but with each complication the learning curve becomes more flat. Table II presents the most important postoperative complications. Besides these complications, there were two interventions on D0 to repair the integrity of the ventricular septum following its rupture and patch dislocation, and in two cases the wound was repaired. There were 4 deaths recorded in the first 30 days following the intervention: 1 patient developed acute renal insufficiency needing peritoneal dialysis, upper digestive hemorrhage, paralytical ileus and died on D20; the 2nd patient developed supraventricular arrhythmia, motor agitation and severe respiratory infection and died on D10; the 3rd patient developed severe right ventricular failure and died on D3; the last patient died on D1 due to multiple organ failure which has been present before the intervention. All these cases presented a respiratory infection, marked as a significant risk factor for early mortality by Fisher's test (p=0.0032). The incidence of early mortality was 2% in our study. The average number of days spent in the Intensive Care Unit was 7±5.8 days.

The most important late postoperative complications in patients who underwent correction of Tetralogy of Fallot is residual pulmonary regurgitation, dilatation and dysfunction of the right ventricle due to pulmonary regurgitation and possibly due to the associated tricuspidal regurgitation, residual obstruction of the RVOT, stenosis or hypoplasia of the branches of the pulmonary artery, sustained ventricular tachycardia, sudden cardiac death, atrioventricular block, atrial flutter/fibrillation, progressive aortic regurgitation [3] (Table III). According to the data presented in Table III, moderate/severe pulmonary regurgitation and reobstruction of the RVOT represented the two most important indications for post-correction reintervention. Thus, the pulmonary valve was replaced in 6 cases and the RVOT was reconstructed in 8 cases. The right ventricle-pulmonary artery conduits got obstructed and were replaced in 3 cases.

The rate of reinterventions was 20.4% during the follow-up period. As far as mid-term mortality is concerned, there were 5 postoperative deaths recorded. One occured at 3 months, due to the thrombosis of the systemic-pulmonary shunt. Three deaths occured at 12, 21 and 26 months respectively, most probably due to pulmonary infections. An other death occured due to a malignant arrhythmia 42 months after the operation and the last one was a sudden cardiac death, 36 months after the operation. Late mortality was 2.5% in our study group. Taking into consideration the total number of deaths (n=9), the survival rate until August 2011 is 95.3% (Figure 1). According to the Kaplan-Meier curve the survival rate at 1.16 years is 96.4%, at 2.7 years 95%, at 3.08 years 93.1% and at 6 years 90%.

Discussions

The primary surgical correction of Tetralogy of Fallot in newborns and infants is relatively new in our country (beginning in 2005), compared with the worldwide experience, therefore it is difficult to compare and extrapolate our results, with an average follow-up time of 32 months (range 4–64 months). The actual survival rate is 93.9% and the Kaplan-Meier curve estimates the survival at 6 years to be 90% (Table IV). Table IV demonstrates that our unit's performance is comparable with that of many prestigious hospitals from around the world.

The current tendency in the surgical management of Tetralogy of Fallot is that of an early approach, in the first months of life, in order to avoid deaths caused by the natural evolution of the disease and secondary complications caused by hemodynamic imbalances and generalized hypoxia. Although the surgical decision regarding the patients' age is still a controversial subject, more and more studies infirm the increased risk of cardiac surgery in newborns. An early anatomical correction seems to conserve the mechanical and electrical function of the myocardium, with a positive effect on angiogenesis and alveologenesis in conditions of insufficient pulmonary perfusion [9]. Our study reveals a decrease in the average age of patients undergoing surgery in the last two years, compared with the 6-year average (32 months compared to 37 months). The usage of monovalved patches in the enlargement plasties of the RVOT, compared with an earlier period when the

patches were unvalved, led to a decrease in the number of residual pulmonary insufficiencies in the past years, a condition which leads in time to the dilatation of the right ventricle, loss of function of the right ventricle and needs reintervention for its correction.

Conclusions

Early surgical intervention represents the only chance of survival for children with Tetralogy of Fallot, the ideal age for the correction being between 6-12 months. In the symptomatic newborn the palliative intervention is recommended only when hypoplastic pulmonary branches are present, with a Z score <-2 compared with accepted normograms. If 10 years ago palliative intervention was the elective treatment for infants younger than 1 year, currently the optimal age for the intervention is 6 months, due to the evolution of surgical technique, extracorporeal circulation and the attitude of intenstive care physicians.

A complex evaluation of the preoperative functional and morphological status of each patient, as well as the close collaboration between the pediatric cardiologist, anesthesist and operating team, improve the prognosis of the patient.

Long-term follow-up, especially with the help of echocardiography (the elective investigation in this pathology) seeks to identify late, inevitable complications - residual lesions, pulmonary insufficiency, right ventricular dysfunction, which influence quality of life and will command the need for a reintervention.

A palpable benefit of surgical correction is the fact that 79% of the 193 studied patients are completely integrated socially in kindergardens and schools, with physical and intellectual performances perfectly between normal parameters. The other 21% still need permanent assistance, mainly due to the associated comorbidities prior to the correction, such as genetic syndromes or neurological disorders.

Although we cannot draw a clear conclusion regarding the long-term results of the applied surgical treatment, the short- and mid-term statistical indicators are satisfying, and this is the beginning of a study of a higher magnitude.

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