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ORIGINAL ARTICLE

Repair of Tetralogy of Fallot in Children Less Than 4 kg Body Weight

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Abstract We reviewed our experience of surgical repair of Tetralogy of Fallot (TOF) in children weighing less than or equal to 4 kg to compare outcome of early palliation versus complete repair as the initial surgical approach. Seventy-six patients, weighing ≤4 kg, with TOF surgery between January 2005 and September 2013 were included in this single-center retrospective study. Twenty-five patients who underwent initial shunt procedure followed by later full repair were compared to 51 patients who had primary full repair for differences in baseline characteristics and outcomes. Shunt group patients had lower body weight, 2.76 ± 0.69 versus 3.11 ± 0.65 (kg), $p = 0.03$, and lower preoperative oxygen saturations, 82 ± 7 versus 90 ± 6 (%), $p = 0.0001$, than full repair group. A higher number of surgical procedures per patient was recorded in shunt patients, 2.29 ± 0.59 versus 1.27 ± 0.49, $p = 0.00002$. Thirteen of 51 patients in the full repair group required a repeat surgery. Catheterization procedures were performed in 12 patients in shunt and in 15 patients in full repair group, with interventional angioplasty in three and 11, respectively, $p \geq 0.05$. Two patients, both in the shunt group, died after the surgery. Early full repair had longer hospital stay but significantly less hospitalizations 1.95 ± 1.3 versus 2.5 ± 1.4, $p = 0.03$. Initial complete repair of TOF in small children yielded favorable outcome with significantly less surgical procedures and subsequent hospitalizations. Cath laboratory re-interventions for residual defects were similar after both surgical approaches, and type of initial surgery does not predict freedom from re-intervention.

Keywords Tetralogy of Fallot · Cyanosis · Shunt · Congenital · Palliation

Introduction

Tetralogy of Fallot (TOF) is the most common type of cyanotic congenital heart disease (CHD), occurring in 3–6 infants for every 10,000 births and accounting for one-third of all CHD in patients younger than 15 years. Surgery is the only definitive treatment. Most patients with TOF become cyanotic shortly after birth; the progression and severity of cyanosis depend on the degree of right ventricular outflow tract (RVOT) obstruction. Without surgery, the natural progression of the disorder portends a poor prognosis. The ideal timing of complete surgical repair is dependent upon numerous variables, including symptoms and any associated lesions.

Based on clinical presentation and patient-specific anatomy, the surgical procedure can be either a full repair in one stage or an initial palliative procedure to increase pulmonary blood flow, followed by subsequent complete correction. Recent studies have shown, however, that complete repair is preferably done at or about 12 months of age [1]. Most surgically treated patients born with TOF now thrive well into their adult years.

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Currently, in asymptomatic patients, the trend is to perform a complete surgical procedure (often electively) before the age of 1 year and preferably by the age of 2 years. However, certain situations, including the presence of an anomalous coronary artery, multiple ventricular septal defects, small pulmonary arteries, or very low birth weight, may add further complexity to surgical planning.

The treatment of neonates and small children with symptomatic TOF requiring surgical intervention early in life remains controversial. Kanter et al. [4] showed that shunting or primary repair of neonates with symptomatic TOF provides equivalent long-term mortality and results. Other studies have shown superior results for primary complete repair [9]. It has also been demonstrated that primary repair avoids prolonged right ventricular outflow obstruction and the subsequent right ventricular hypertrophy and prolonged cyanosis [4].

In this study, we examined the approaches to and results of surgical repair of TOF in patients with a body weight of 4 kg or less at our institution. We hypothesized that the initial approach (shunt vs. complete repair) would be associated with differences in clinical outcomes.

Patients and Methods

This study was approved by the institutional review board (IRB) at Columbia University. All patients with the diagnosis of TOF with a body weight of up to 4 kg who underwent surgical repair from January 2005 through September 2013 at Morgan Stanley Children's Hospital of New York-Presbyterian were included in this analysis. Four kilograms body weight was chosen as the cutoff point, because there was greatest variability in the surgical approach to these patients, who account for a disproportionate share of early re-intervention in TOF. Inclusion criteria were based on surgical diagnosis of TOF. Patients with TOF who had major aortopulmonary collateral arteries, were excluded from this study. All patients were referred for surgery due to symptoms of intermittent or continuous cyanosis.

Patients were categorized into two groups based on the surgical approach. Shunt group comprised patients who initially were palliated with a systemic-to-pulmonary shunt [Blalock-Taussig (BT) shunt or central aortopulmonary shunt]. In complete repair group, patients had initial complete repair of TOF.

The surgical plan was determined by the operating surgeon. Surgical decision making was individualized and involved factors such as the urgency of the operation, size of the pulmonary arteries, additional anatomic variations, and surgeon preference.

The primary outcome in our study was mortality, and the secondary outcomes were surgical and percutaneous re-intervention.

Operative Technique

The operative techniques for aortopulmonary shunts varied according to surgeon and patient symptoms. Unstable patients underwent operation on cardiopulmonary bypass (CPB). Patients with right-sided aortic arch and/or small aortic arch branches underwent a central shunt. Otherwise, a BT shunt was performed through a right thoracotomy or midsternotomy based on surgeon preference. All patients who underwent initial palliative shunting underwent a complete repair in the course of a few months, with division of the shunt and repair of any shunt-related pulmonary artery distortion or stenosis if needed.

For complete repair, cardiopulmonary bypass was established with bicaval cannulation using moderate hypothermia and cold blood cardioplegic arrest. Deep hypothermic circulatory arrest (DHCA) was additionally employed sporadically only during the early period of the study. The ventricular septal defect was closed through either the right atrium or right ventricle. In order to address the RVOT obstruction, patients underwent either transannular patch or a valve sparing technique, or a right ventricle to pulmonary artery conduit, depending on anatomic factors (e.g., a coronary crossing the RVOT) and on surgeon's preference.

Statistics

Outcomes were analyzed as either continuous or categorical variables. Continuous variables are presented as mean ± standard deviation and were compared using a Student's t test in a univariate analysis of variance model. Categorical variables were compared using the Fisher's exact test. In all comparisons, a p value <0.05 was considered significant.

Results

Seventy-six patients were included the study, 25 in the shunt group and 51 in full repair group. Patients' baseline characteristics are summarized in Table 1. Patients in the shunt group had smaller body weight on average than the complete repair group, 2.76 ± 0.69 versus 3.11 ± 0.65 kg, $p = 0.03$. However, no differences were seen between groups with respect to the calculated body surface area 0.20 ± 0.05 versus 0.21 ± 0.03 m2 ($p = 0.7$). Preoperative oxygen saturation was significantly lower in the

Table 1 Demographic data

Variable	Shunt group ($n = 25$)	Full repair group ($n = 51$)	p value
Age (days) (range)	20.2 ± 20.3 (2–89)	31 ± 30.7 (2–123)	0.1
Weight (kg) (range)	2.76 ± 0.69 (1.7–3.8)	3.11 ± 0.65 (1.7–4.0)	0.03
Body surface area (m2)	0.20 ± 0.05	0.21 ± 0.03	0.7
Preoperative oxygen saturation (%)	82 ± 7	90 ± 6	0.0001
Number of surgical procedures/patient	2.29 ± 0.59	1.27 ± 0.49	0.00002
Follow-up period (days)	2029 ± 806	1661 ± 885	0.08
Mortality	2	0	0.1
Length of stay (first) (days)	17.7 ± 17	21.7 ± 20.7	0.4
Number of hospitalizations	2.5 ± 1.4	1.9 ± 1.3	0.03
Patients on preoperative prostaglandin	12	17	0.3
Syndromes and major congenital anomalies	9	8	NA
	Down 5, DiGeorge 2, Noonan 1, Omphalocele 1	Down 4, DiGeorge 3, Charge 1	

shunt group (82 ± 7 %) than in the full repair group (90 ± 6 %, $p = 0.0001$).

In the shunt group, there was notable variability in operative technique. Of 25 patients initially treated with a shunt, 16 underwent a BT shunt and nine underwent a central shunt. Of 16 BT shunts, eight were performed through a thoracotomy and 8 through sternotomy (3 with CPB support). Of nine central shunts, one was performed via thoracotomy and eight via sternotomy (five with CPB support).

A repeat shunt procedure to revise an occluded shunt was required in 2/25 patients (8 %). One patient in the complete repair group needed extracorporeal membrane oxygenator (ECMO) support for severe hypoxemia due to reperfusion injury of the lung after the second surgery, but eventually recovered. No mortality was recorded in the complete repair group.

The approach to close the ventricular septal defect either through the atrium or a ventriculotomy was based on surgeon's preferences. There was no difference between the groups in the incidence of transventricular VSD closure.

All patients survived and are alive and well in the full repair group. Seven patients underwent valve sparing repair technique, four underwent right ventricle to pulmonary artery conduit, and the rest were treated with a transannular patch. Sixteen patients in this group underwent deep hypothermic circulatory arrest in order to accomplish the full repair. This technique was not utilized after November 2008. Three patients in the full repair group had delayed sternal closure due to hemodynamic instability or severe edema that precluded chest closure at the time of the surgery.

In the shunt group, the average time between the initial shunt and the later full repair was 307 ± 219 days. In this group, no surgery was needed after the second complete repair. In the full repair group, an additional surgical re-intervention was performed in 13 patients (25 %). The second procedure was PA plasty in six patients, RV-PA conduit insertion in two patients, and RVOT patch (revision or insertion) in five patients. Two patients needed a third procedure: addition of a BT shunt in one patient and a RVOT patch and PA plasty in one patient. Despite these surgical re-interventions in the full repair group, this group had significantly lower number of total surgical procedures per patient compared with the shunt group, 1.27 ± 0.49 versus 2.29 ± 0.59, $p = 0.00002$.

All patients were followed with regard to diagnostic and interventional catheterization procedures performed for diagnostic purposes or for treatment of residual defects. The follow-up cardiac catheterization data are summarized in Table 2. Intervention at the time of catheterization was defined as angioplasty of pulmonary arteries or right ventricle outflow tract, or stent placement. No difference was seen between the groups in total number of procedures or procedures per patient, either diagnostic or interventional. The type of initial surgical approach (shunt vs. full repair) had no effect on the rate of percutaneous re-intervention.

To determine association between age, weight, BSA, and preoperative oxygen saturation with angioplasty intervention after surgery, we compared these variables in each group based on angioplasty status (Table 3). Only young age in the shunt group was associated with post-operative angioplasty intervention, and no other associations were found in these parameters between patients with and without angioplasty (Table 3).

The shunt group had 4 days shorter initial hospital stay compared with the complete repair group. This difference was not statistically significant ($p = 0.4$); however,

Table 2 Postoperative catheterization data (diagnostic and interventional)

Variable	Shunt group ($n = 25$)	Full repair group ($n = 51$)	p value
Number of patients undergoing catheterization procedures			
Diagnostic	12 (48 %)	15 (29 %)	0.1
Angioplasty	3 (12 %)	11 (21 %)	0.3
Total catheterization procedures			
Diagnostic	16	27	0.4
Angioplasty	7	21	0.3
Number of catheterization procedures per patient	0.64 ± 0.81	0.53 ± 1.01	0.6
Number of angioplasty procedures per patient	0.24 ± 0.52	0.41 ± 0.88	0.3

Table 3 Comparison between patients with or without need for postoperative angioplasty procedure

	Angioplasty	No angioplasty	p value
Shunt group			
Age	15.1 ± 11.6	41 ± 34	0.01
Weight	2.6 ± 0.72	3.04 ± 0.52	0.3
Body surface area	0.2 ± 0.06	0.2 ± 0.02	0.9
Preoperative O2 saturation	83 ± 8	80 ± 6	0.9
Full repair group			
Age	32.4 ± 32.3	26.9 ± 26.3	0.5
Weight	3.17 ± 0.6	2.95 ± 0.7	0.3
Body surface area	0.21 ± 0.03	0.2 ± 0.03	0.1
Preoperative O2 saturation	90 ± 6	92 ± 7	0.4

comparison of overall number of subsequent admissions (surgical and medical) revealed a significant advantage in the complete repair group with fewer hospitalizations, 1.9 ± 1.3 versus 2.5 ± 1.4, $p = 0.03$.

Of the 25 patients who underwent initial shunt procedure, two died. One patient with Noonan syndrome had shunt thrombosis on the first postoperative day and underwent a shunt revision, following which she became hypotensive and developed multi-organ failure; eventually support was withdrawn, and the patient died on postoperative day 25. The second patient died on postoperative day 17 due to ventricular arrhythmia which followed sepsis and hypoglycemia.

Discussion

The ideal repair for TOF is performed when the patient is asymptomatic or mildly symptomatic at a later age, outside of the neonatal period. In such a patient, a complete repair is performed electively. The main controversy regarding surgical approach occurs when a cyanotic newborn or infant presents for surgery. In this scenario, there are two possible options: a staged surgery, with palliative systemic-to-pulmonary shunt followed by complete repair at an older age, or an initial complete repair. Each strategy has advantages and disadvantages, and there is a wide variation in the preferred approach between different centers. Decision making becomes even more difficult when specific factors such as age and weight of the patient, severity of the disease and its symptoms, presence of additional defects or comorbidities, and the specific anatomy of each patient play a role. In this study, we compared the two main approaches to TOF repair in small infants, with a focus on the outcome and later re-interventions, to determine whether one approach is superior to the other.

The shunt group by definition requires two surgeries, and the expectation of the primary complete repair is a single and definitive surgery. Some patients in the full repair group needed a later revision, which increased the number of surgical procedure from the expected one per patient to 1.27. The majority of these revisions were performed in the early period of our study, reflecting technical improvements and potential elimination of the need for any future revision or angioplasty procedure after the initial full repair. Given this fact, it is possible that in selected patients, a full initial procedure would be preferred as it will decrease the number of total procedures, along with minimizing future hospitalizations and their inherent risk.

Multiple studies have demonstrated advantages of a certain approach over another in different repair performed at earlier age in many centers owing to improved surgical technology.

In a study published by Kanter et al. [4] in patients with symptomatic neonatal TOF, mortality and other outcomes measured were equivalent between patients undergoing initial shunt palliation and those undergoing primary complete repair. In their series, shunted patients had fewer transannular patch repairs despite having more emergent

initial operations. This pattern was not seen in our study as the majority of shunted patients underwent repair with transannular patch. In a study evaluating repair of TOF in the less than 4-month age group and neonates younger than 28 days with duct-dependent pulmonary circulation or severe hypoxemia, Tamesberger et al. [11] showed good outcomes for early primary repair. With improving surgical techniques, many groups have adopted the complete initial repair approach at different age or weight cutoffs. Although a shunt procedure offers an initial palliation for TOF patients, it comes at a cost of significant morbidity and mortality [2, 8]. Once a breakthrough procedure saving lives of blue babies, its advantages are offset in the current era with a complete repair. In a large study analyzing Society of Thoracic Surgeons [STS] data, primary repair in the first year of life was shown to be the most prevalent strategy [1]. In the STS data, it is notable that ventriculotomy with transannular patch remains the most commonly used technique, both for primary repair and for repair following palliation [1]. This type of surgical repair was the dominant repair type in the complete repair group in our series as well. Regardless of which technique was used initially, patients undergoing TOF repair have a high overall rate of re-intervention, with corresponding additional risk.

Another major factor in comparing the two surgical approaches is the association between the repair type and overall mortality. Several published studies have shown low mortality and morbidity in complete primary repair of TOF [10], especially when the early one-stage repair was performed in symptomatic infants [6]. In our study, perioperative mortality was identified only in the shunt group and not in the full repair group. In this retrospective series, no conclusions can be drawn as to whether the primary shunt approach or the severity of illness in the shunt group patient population led to this difference in mortality. Patients in this group likely were selected for a shunt due to case complexity and lower weight, as well as severity of symptoms, as indicated by the lower preoperative oxygen saturations when compared to the complete repair group. The possibility of an off-pump aortopulmonary shunt makes such an approach seemingly favorable in severely ill patients and might in some cases reduce the risks associated with surgery.

Early one-stage complete repair was also suggested by Park et al. [7]. In that study, the early complete repair was associated with no increased risk of reoperation or re-intervention in the short term. It was also demonstrated that the pulmonary valve annulus is likely to be preserved when it is repaired at an early age and the early total repair may be better for pulmonary arterial growth than a staged repair. Such an approach has been adopted in selected cases in our study population in recent years. The early one-stage repair of TOF was supported also by Pigula et al. [9]. In one study assessing the influence of perioperative factors on outcomes in children younger than 18 months undergoing repair of TOF, it was found that both younger age at repair and previous palliative procedures were associated with longer duration of stay in the intensive care unit [3]. In a midterm outcome analysis done by Kantorova et al. [5], good outcome in terms of morbidity rate and re-intervention was expected when elective primary repair in asymptomatic patients was delayed beyond 3 months of age. In symptomatic patients, primary repair was performed irrespective of age, weight, and preoperative state. In our study, length of hospital stay was nonsignificantly shorter in the shunt group. This difference, even if significant, however, would have been offset by a significantly higher number of surgical procedures per patient and more frequent later hospitalizations in this group.

With improving catheterization techniques, percutaneous interventions to dilate the right ventricular outflow tract or a pulmonary artery have become an adjunct to surgical procedures. In some cases, these interventions provide a means to optimize the surgical results. Surgeons may now feel more permissive of residual defects or imperfections resulting from early single-stage surgery in a dynamic growth situation when a subsequent nonsurgical correcting maneuver is available by percutaneous interventions. In our patients, the incidence of catheterization either diagnostic or interventional had no correlation with type of surgical approach.

Limitations of the Study

This study is limited by small sample size and by its retrospective nature, which is inherently biased. In addition, variability in surgical approach may have confounded the analysis; shunts were approached through a variety of techniques; and deep hypothermic circulatory arrest was infrequently used for complete repair in the early study period, and valve sparing techniques in the later. The era effect includes also personnel change during the study time. In addition, there has been significant evolution of both surgical and transcatheter techniques during the time frame of the study, which may have impacted patient management.

Conclusions

Treatment of TOF is still evolving in the face of improving surgical techniques and availability of percutaneous procedures. The complete initial repair has a favorable outcome in terms of survival and hospital stay and no association with subsequent percutaneous intervention

more than the shunt group in patients with TOF under 4 kg body weight. This approach is associated with less frequent overall surgical procedures and cardiac-related admissions. Availability of nonsurgical interventions comprises an important cornerstone supporting a single-stage complete surgery as opposed to stage with palliation first. The staged approach with initial palliation might be advantageous in severely sick patients or in other extreme situations in which an acute palliation or a salvage procedure is necessary.

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