Surgical outcomes in the treatment of patients with tetralogy of Fallot and absent pulmonary valve

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Abstract

Objective: Tetralogy of Fallot and absent pulmonary valve (TOF/APV) is associated with significant pulmonary artery dilatation and airway compression. Treatment of infants presenting with respiratory symptoms early in life is associated with high mortality (20—60%). We aim to report our results and identify factors associated with survival and prolonged ventilation. Methods: We performed a retrospective review of 62 consecutive patients following repair of TOF/APV (1982—2006). Median age at repair was 1.4 years (1 day—35 years). Twenty patients required preoperative intubation. Results: Sixty-one patients underwent complete repair. Thirty-three patients underwent pulmonary artery plication (n = 15) or reduction (n = 18). The right ventricular outflow tract (RVOT) was reconstructed with valved conduit (n = 31), bioprosthetic valve (n = 18), monocusp (n = 8), or transannular patch (n = 4). There were three perioperative and five late deaths. All perioperative deaths were in neonates and before 1995. Five- and ten-year survival was 93 ± 4% and 87 ± 5%. Mean ventilatory requirements for neonates, infants, and children 1 year were 36 ± 35, 8 ± 8, and 2.6 ± 2.4 days (p < 0.0001). On multivariable analysis, significant factors associated with prolonged ventilation were neonates (p < 0.0001) and preoperative mechanical ventilation (p = 0.088). Eight airway reinterventions were needed in seven infants with persistent postoperative airway compromise, pulmonary artery suspension (n = 4), innominate artery suspension (n = 2), and lobectomy (n = 2). Freedom from RVOT reoperation was 89 ± 5% and 59 ± 9% at 5 and 10 years. There were no significant risk factors for time-related survival or RVOT reoperation on multivariable analysis. Conclusions: In contrast to children and adults with TOF/APV, neonates and small infants presenting with respiratory symptoms require prolonged ventilation and additional reinterventions for airway compression. Our current surgical approach which includes reduction and suspension of pulmonary arteries, reconstruction of a competent RVOT, and aggressive postoperative ventilatory management to relieve airway obstruction offers satisfactory outcomes.

Keywords: Congenital heart disease; Tetralogy of Fallot; Pulmonary Insufficiency; Respiratory failure; Valve replacement

1. Introduction

Tetralogy of Fallot (TOF) associated with absent pulmonary valve (APV) is a rare variant that comprises 3—6% of all patients with TOF. In addition to the typical intracardiac abnormalities associated with TOF (malalignment ventricular septal defect, stenosis of right ventricular outflow tract, and right ventricular hypertrophy), patients with TOF/APV have rudimentary or absent pulmonary valve leaflets with free pulmonary insufficiency. Most importantly, neonates and infants presenting with TOF/APV commonly have characteristic aneurysmal dilatation of the pulmonary artery and its branches which can cause compression of the tracheobronchial tree. Consequently, TOF/APV patients frequently require preoperative ventilatory support and often need early neonatal surgical repair [1—3].

Surgical treatment of neonates and infants with TOF/APV has been associated with increased postoperative respiratory complications and hospital mortality [4—11]. Several modifications of surgical techniques have emphasized reduction of dilated pulmonary arteries, establishment of pulmonary valve competency using valved conduits, and relief of obstruction of the tracheobronchial tree by means of suspension of the compressing pulmonary arteries, translocation of the pulmonary artery, or even segmental resection of the lung [10—16]. The surgical modifications noted above and recent advances in postoperative care and ventilatory...
management of neonates and infants have all contributed to improved surgical outcomes in patients with TOF/APV.

The purpose of this study is to review the operative results following surgical repair of children with TOF/APV at our institution and to outline our current treatment strategy in this difficult group of patients.

2. Patients and methods

Clinical, operative, and outcome data were collected retrospectively. Institutional review board approval was obtained prior to chart reviews and individual consents were waived.

From July 1982 to February 2006, 62 patients underwent surgical repair for tetralogy of Fallot with absent pulmonary valve at the Hospital for Sick Children and Toronto General Hospital in Toronto. There were 20 males and 42 females. Median age at repair was 1.4 years (range, 1 day—35 years), and median weight at repair was 8.6 kg (range, 2.4—73.0 kg). Age at initial repair included 11 neonates, 18 infants (1 month—1 year old), 30 children (1—18 years old), and 3 adults (>18 years old). While 6/33 patients (24%) in the earlier 12 years of our experience (prior to 1995) were infants, 23/31 (72%) of patients in the later 12 years of our experience were infants. Twenty patients had respiratory distress requiring preoperative intubation including 11 neonates. Three patients had undergone previous palliation including pulmonary artery banding (n = 1), left modified Blalock—Taussig shunt for isolated left pulmonary artery (n = 1), and attempted repair in a different country (n = 1). The clinical profile of the entire cohort is summarized in Table 1.

2.1. Operative technique

All procedures were performed though midline sternotomy. Cardiopulmonary bypass was established via standard aortic and bicaval venous cannulation. The left ventricle was decompressed by venting through the patent foramen ovale (or through an opening that was created in the atrial septum). Mild hypothermia (32—34°C) and antegrade cold blood cardioplegia were used for myocardial protection.

Complete repair was performed in 61/62 patients while one patient had plication of the dilated pulmonary arteries without closure of the ventricular septal defect (VSD). Enlargement of the right ventricular outflow tract (RVOT) was done by resecting the hypertrophied muscle bundles through a trans-atrial approach and through the infundibular incision that was made in the RVOT to serve as the site for the right ventricle—pulmonary artery (RV—PA) conduit or for the infundibular patch.

The approach to pulmonary artery dilatation varied with the age of patients, the degree of compression of the airways, and with the era of surgery. Twenty-nine patients did not have any intervention on their central pulmonary arteries. Fifteen patients underwent pulmonary artery plication (unilateral n = 11 or bilateral n = 4). Eighteen patients had reduction of the pulmonary arteries by excising elliptical strips of the pulmonary artery wall (6 anterior, 6 posterior, and 6 combined anterior and posterior).

The VSD was closed using a Dacron patch. The defect was usually closed trans-atrially by retracting the tricuspid valve leaflets. Following closure of the VSD, the left heart was deaired and the aortic cross clamp released. The remaining reconstruction was performed with an empty beating heart to minimize myocardial ischemic time.

Right ventricle—pulmonary artery continuity was reconstructed with a valved conduit (n = 31), bioprosthetic valve (n = 18), monocusp (n = 8), or transannular patch (n = 4).

Additional procedures included reimplantation of left pulmonary artery (LPA) into the main pulmonary artery for isolated LPA (n = 6) and multiple muscular VSD closure (n = 2). Our surgical approach in neonates and infants with tetralogy of Fallot and absent pulmonary valve has evolved with time into our current strategy that includes complete intracardiac repair with VSD closure, infundibular resection, reduction of the dilated pulmonary arteries (anterior, posterior, or both based on the degree of dilatation), reconstruction of the RVOT with valved conduit (homograft or Contegra bovine jugular vein conduit), and suspension of the left pulmonary artery to the chest wall upon closure of the chest. We tend to leave the patent foramen ovale open in infants and neonates because of the restrictive right ventricle physiology, and often the chest is left open perioperatively with delayed closure done in the intensive care unit within few days of surgery.

Intraoperative trans-esophageal echocardiography (TEE) was done in all patients to assess the quality of repair. Complete operative data are summarized in Table 2.

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<td><strong>Operative details for all patients</strong></td>
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<td>RVOT reconstruction technique</td>
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<td>Incomplete repair (VSD left open)</td>
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<td>Reimplantation of isolated left pulmonary artery</td>
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<td>Closure of multiple muscular ventricular septal defects</td>
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<td>Chest left open</td>
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<td>Cardiopulmonary bypass time (min)</td>
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<td>Aortic cross clamp time (min)</td>
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2.2. Follow-up

Follow-up data were obtained from review of recent office visits at the Hospital for Sick Children and from our database that is updated continuously using written communications with the patients’ outside cardiologist. The mean follow-up was 7.97 ± 6.75 years (range, 1 day–21.6 years) and was complete.

2.3. Statistical analysis

All the data were analyzed with the SAS software program (version 9; SAS Institute Inc., Cary, NC). Data are presented as frequency, median with range, or mean ± SD as appropriate, with the number of non-missing values indicated. Unrelated two-group comparisons were done with unpaired, 2-tailed t-tests for continuous variables and χ² or Fisher exact test for categorical data. Predictors of perioperative mortality were identified using multivariable logistic regression analysis. Estimates for long-term survival or freedom from reoperation were made by the Kaplan–Meier method. Differences between survival curves were evaluated with the log-rank statistic.

Cox regression was used to determine the independent predictors of late outcomes. The appropriateness of variable transformations was determined by means of univariate analysis. Variables with a univariate p value of less than 0.05 or those with known biologic significance but failing to meet this critical χ² level were submitted to multivariable models.

3. Results

3.1. Operative results

Sixty-one patients underwent complete repair. Mean cardiopulmonary bypass (CPB) time was 137 ± 49 min and mean aortic cross clamp time was 53 ± 20 min. Three patients required operative revision and reinstitution of cardiopulmonary bypass, one patient for uncontrolled bleeding from the left atrial appendage, one patient for residual RVOT obstruction following transannular patch that was revised with a homograft, and one patient with residual RVOT following homograft RV–PA conduit that was revised with the use of bioprosthesis.

Following surgery, the chest was left open in 11 patients who required delayed sternal closure in the intensive care unit few days postoperatively. Major postoperative complications included reexploration for bleeding (n = 1) and pacemaker implantation (n = 1).

Several infants with postoperative respiratory distress owing to compression of the airways by the dilated pulmonary arteries required further surgical interventions to relieve the compression. These interventions were needed in seven patients and included pulmonary artery suspension (n = 4), innominate artery suspension (n = 2), and right upper and middle lobectomy (n = 2). These procedures were not needed in any patient >3 months old.

Median ICU stay following surgical repair was 4 days (range, 1–102 days). Mean ICU stay for neonates, infants >30 days old and children ≥1 year old was 40 ± 39, 10 ± 9, and 3 ± 3 days, respectively (p < 0.0001).

Operative mortality, defined as death within the initial postoperative hospitalization or within 30 days from surgery, was 4.8% (3/61). All deaths were in neonates aged 3, 10, and 15 days. One patient was in shock preoperatively and was taken emergently to the operating room but couldn’t be weaned off CPB, one neonate expired on the 2nd postoperative day from severe myocardial dysfunction, and one final death was in a neonate who underwent pulmonary artery plication without complete intracardiac repair and didn’t survive to discharge. There were no deaths among infants >30 days old or in older children. Operative mortality was 9% prior to 1995 and has been zero since 1995.

Several variables were analyzed to assess if they were risk factors for operative mortality. These variables included the age, sex, and weight of patients, the duration of cardiopulmonary bypass and aortic cross clamp, preoperative respiratory compromise requiring ventilation, and the era of surgery. None of these variables was identified as an independent risk factor on multivariable analysis.

Median postrepair ventilatory requirement was 3 days (range, 1–93 days). Mean ventilatory requirements for neonates, infants >30 days old and patients ≥1 year old were 36 ± 35, 8 ± 8, and 2.6 ± 2.4 days, respectively (p < 0.0001). On multivariable analysis, significant variables associated with longer ventilatory requirement were neonatal age (p < 0.0001) and preoperative ventilation (p = 0.088).

3.2. Late results

During the follow-up period there were five late deaths. Two deaths were cardiac, sudden death (n = 1) and death following reoperation for RV–PA conduit change (n = 1). The remaining deaths were non-cardiac, malignancy (n = 1), viral pneumonia (n = 1), and septic shock (n = 1).

Overall survival at 5 and 10 years was 93 ± 4% and 87 ± 5%, respectively (Fig. 1), 4/5 late mortalities were in patients undergoing initial surgery as neonates, with the remaining

![Fig. 1. Time-related survival stratified by age groups (infants vs others).](image-url)
mortality in a patient who had her surgery at age 5.8 years and died following her conduit change (Fig. 1).

Eighteen patients underwent 22 reoperations during the follow-up period. Those included pulmonary valve replacement (n = 12), RV-PA conduit change (n = 8), and resection of RVOT aneurysm (n = 3). Freedom from reintervention at 5 and 10 years was 89 ± 5% and 59 ± 9%, respectively (Fig. 2).

Using the Cox multivariable regression model, we were unable to identify any significant demographic or operative factors for long-term survival or freedom from reoperation.

4. Discussion

The management of neonates and small infants with tetralogy of Fallot and absent pulmonary valve associated with tracheo-bronchial compression remains a challenge. The mortality for neonates and infants with TOF/APV remains high in most reported series despite the dramatic reduction in mortality for infants undergoing repair of other complex congenital heart defects in recent years [4—11]. In multiple previous reports, a distinction has been made between TOF/APV patients who present early in life with severe respiratory symptoms and those who present later in life and usually follow a more benign clinical course similar to that of standard TOF patients [4—11].

Our treatment strategy in the past 24 years has evolved to include several modifications in operative technique and postoperative respiratory management in an effort to enhance survival in this difficult group of patients. Although improved perioperative care has contributed to increased infant survival, we believe that our surgical modifications have played an essential role in improving treatment outcomes.

4.1. Operative management

There are two areas of debate in the surgical treatment of children with TOF/APV related to the management of dilated pulmonary arteries and to the management of the pulmonary valve.

As airway compression plays a pivotal role in postoperative morbidity; several groups of surgeons have recommended different palliative maneuvers to eliminate those complications. These palliative maneuvers included anterior and posterior plication of the dilated pulmonary arteries, reduction of the pulmonary artery by excising parts of the posterior or anterior walls, suspension of pulmonary artery to the retrosternal fascia, translocating the pulmonary artery anterior to the aorta by fully mobilizing the branch pulmonary arteries away from the airways with the Lecompte maneuver, or even complete removal of the entire main pulmonary artery and the majority of the branch pulmonary arteries with either posterior reconstruction of the bifurcation and homograft placement or placement of a bifurcated pulmonary homograft [4,11—17].

Our current strategy in infants with TOF/APV is to reduce the size of all dilated central pulmonary arteries. The procedure is individualized to each infant based on the degree of aneurysmal dilatation and airway collapse. In the more severe cases, we perform elliptical excision from both posterior and anterior walls of the branch pulmonary arteries. We do not perform the Lecompte maneuver routinely but recognize its potential value in patients with airway compression [13]. In addition, we routinely suspend the left pulmonary artery to the retrosternal fascia after completion of surgery or at the time of delayed chest closure in the intensive care unit.

Another area of controversy is the management of the pulmonary valve and the reconstruction method of the right ventricular outflow tract. While most surgeons agree that reduction in central pulmonary artery size is important, there is less agreement regarding the optimal method of RVOT reconstruction. Some surgeons have advocated utilization of a valved conduit while others suggested that in the absence of pulmonary hypertension, the use of a transannular patch is sufficient [8,10,11,15,16]. Transannular patch with or without a monocusp valve construction was utilized earlier in our series and was not identified as a risk factor in the current analysis. Nevertheless, it is our current operative strategy to implant a competent pulmonary valve (usually a valved conduit in neonates and infants) in order to eliminate pulmonary valve regurgitation. This strategy is predicated on the assumption that an incompetent pulmonary valve contributes to pulmonary artery dilation and that prevention of pulmonary insufficiency reduces the risk of long-term arrhythmias and late right ventricular dysfunction [18]. In the more immediate setting, pulmonary valve insertion may improve the early postoperative hemodynamics and diminish the incidence of persistent pulmonary artery dilatation and bronchial compression through elimination of pulmonary artery pulsatility due to the larger pulmonary regurgitant fraction and the increased total pulmonary blood flow [10,19].

4.2. Respiratory management

Airway morbidity differentiates the postoperative recovery and prognosis of neonates from older patients with TOF/APV. The overall survival is closely related to airway pathology being the cause of death. Multiple series have identified the need for preoperative intubation and
ventilation as a risk factor predictive of poor outcome [6,7,11]. While operative strategies aiming to restore pulmonary valve competency and reduce airway compression by the dilated pulmonary arteries are central aspects of the management of those patients; neonates and infants continue to manifest evidence of respiratory compromise and require careful and systematic assessment of etiology of failure and appropriate intervention to assure successful weaning from mechanical ventilation support.

Advances in critical care medicine, modes of ventilation, and better understanding of this disease pathology allowed for successful weaning and eventual hospital survival in all neonates in the last 12 years. Many infants are often placed in the prone position to reduce airway compression, and noninvasive positive pressure ventilation is often utilized following extubation to allow maintenance of airway patency. In patients who fail to make progress, evaluation of persistent airway compression is begun. Bronchoscopy is usually performed to delineate the cause and the site of the airway obstruction and to rule out intrabronchial pathology for collapse. CT scan of the chest can be used to define the intrathoracic anatomy and the relationship between the airway and the vascular structures. In addition, a trans-thoracic echocardiogram and occasionally cardiac catheterization may be needed to rule out any cardiac abnormality such as obstruction of the RVOT, stenosis of the right ventricle—pulmonary artery conduit, or branch pulmonary artery stenosis as the source for respiratory failure.

Once clear understanding of the anatomy and etiology of the failure is made, appropriate intervention is warranted. In our series, eight, respiratory reoperations were performed to relieve the obstruction including left and right pulmonary artery suspension to the sub-sternal fascia, innominate artery suspension, and redo pulmonary artery plication. In addition, patients with TOF/APV commonly have abnormalities of bronchial arborization, with tufts of arteries encircling and compressing the intrapulmonary bronchi that cannot be addressed during surgery and which may contribute to respiratory compromise by causing air entrapment in emphysematous lobes and subsequent compression of the remaining lung [20]. This problem can be addressed by formal lobectomy of the most severely affected lung. In our series, two patients with persistent respiratory distress underwent lobectomy, right middle lobe (n = 1) and right upper and middle lobes (n = 1) with successful relief of their airway compression.

We have not performed tracheostomy in any of our neonates despite prolonged ventilation up to 93 days postoperatively. In addition, we have not used any intrabronchial expandable stents to treat the severe tracheobronchial malacia. Although successful use of those stents has been reported in the literature, we attempt to avoid their deployment as they are limited in terms of total attainable diameter and may require subsequent removal as the child grows [21,22].

4.3. Long-term survival and reoperations

There are little available data concerning the long-term prognosis for children after repair of TOF/APV as follow-up is limited in most reported series. The majority of late mortalities in our series were in patients who underwent surgery as neonates indicating ongoing problems in this age group. The age wasn't a significant factor on multivariable analysis and that may be due to the small cohort and events numbers.

Although survival beyond the perioperative period is very good, patients are likely to present later for reoperation on the right ventricular outflow tract. We were unable to identify predictors of reoperation on multivariable analysis.

While the numbers in our series are small, we did not find any difference in freedom from reoperation between patients undergoing transannular patch, bioprosthetic valve or valve conduit reconstruction of the RVOT. Although younger age at time of implantation of valved conduit is a reported factor for earlier reoperation [23–25], we believe that the advantage of maintaining valve competency and the low operative risk for conduit/pulmonary valve replacement are supportive of our current strategy to avoid persistent pulmonary insufficiency.

4.4. Study limitations

This case series is subject to the limitations inherent in all retrospective observational studies such as selection bias and lack of randomization. In addition, the small cohort size due to the rarity of this disease, and the multiple variables in this series that reflect a development of different surgical approaches related to reconstruction of the RVOT and reduction of the dilated pulmonary artery size, changes in perfusion strategies, and changes in postoperative intensive care all preclude sophisticated statistical analyses and limit the power of the study to identify clinically significant risk factors.

5. Summary

While older children and adults with TOF/APV have smooth postoperative course; neonates and infants presenting with respiratory symptoms continue to require prolonged ventilation and additional reinterventions for airway compression. Nonetheless, current surgical strategy that includes reduction and suspension of the dilated pulmonary arteries, establishment of competent pulmonary valve, along with aggressive postoperative ventilatory management and additional interventions aiming to relieve airway obstruction results in excellent hospital survival in this difficult group of patients. Long-term survival is satisfactory with neonates contributing to the majority of late deaths. Reoperation rate is high and the majority of patients are expected to require RVOT reoperations.

References

Appendix A. Conference discussion

Dr H. Sairanen (Helsinki, Finland): Did you ever consider the LeCompte maneuver in those very, very small children, neonates, who have the worst symptoms?

Dr Alsoufi: The LeCompte maneuver has not been done in this series. However, we do recognize its utility in some infants in whom the surgeon believes that there will be persistent obstruction of the airway despite the reduction and suspension of the pulmonary arteries. Dr Hraska has popularized this technique with excellent results and relatively less frequent need for prolonged ventilation compared to some neonates in our series.

Dr K. Francois (Gent, Belgium): In your late follow-up, have you any idea about the pulmonary pressure in these patients, for instance, in the ones you did redo operations?

Dr Alsoufi: In the original surgery, this information is largely not available since we rely mainly on echocardiogram for diagnosis, and since all patients get an RV–PA conduit regardless to their pulmonary artery pressure opposite to the practice of some surgeons who will recommend transannular patch in infants with no pulmonary hypertension.

As for late follow up, I don’t have this data with me although I am sure it’s available for patients who required angiograms prior to their conduit change.

Dr M. Wojtalik (Poznan, Poland): This is a very tough problem. And there is also a spectrum of malformation. What was your criteria to diagnose absent pulmonary valve syndrome? What criteria did you have to diagnose pulmonary absent valve syndrome?

Dr Alsoufi: In addition to the typical intra-cardiac anatomic findings that are present in all tetralogy of Fallot patients, those patients have rudimentary or absent pulmonary valve leaflets with free pulmonary insufficiency. In addition, those children commonly have the characteristic aneurysmal dilatation of the pulmonary artery and its branches which can cause compression of the tracheobronchial tree.

We rely mainly on echocardiogram for diagnosis at our Institution. Many patients are even diagnosed on pre-natal fetal echocardiogram. In addition, patients usually get a pre-operative CT Scan to delineate the pulmonary arteries anatomy and the degree of airway obstruction.

Dr W. Mrowczynski (Poznan, Poland): The postoperative course of patients you discussed is usually very complicated. For example, we observed prolonged pleural drainage frequently. Did you experience the same problem?