

Primary Repair of Tetralogy of Fallot in the First Year of Life: Impact of Transannular Patch on Operative Mortality and Morbidity

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Objective : There has been much controversy regarding the ideal timing for complete correction of patients with cyanotic tetralogy of Fallot (TOF). The arguments hinge on the morbidity and mortality of the operation. Young age and the requirement for transannular patch (TAP) reconstruction of the right ventricular outflow tract (RVOT) are thought to adversely affect the results of intracardiac repair of TOF.

The purpose of this retrospective study is to evaluate the current results of full repair of TOF in infancy with special stress on the effect of TAP on mortality and morbidity.

Method : From October, 2000 to July, 2004, 30 patients \leq 12 months of age with symptomatic TOF underwent primary full repair of TOF at our hospital. Patients who underwent initial palliative shunt were excluded. Preoperative, operative, and postoperative data were reviewed.

Results : The mean age at repair was 10.1 ± 2.1 months. There was no operative mortality. However, one patient died 15 days following discharge from hospital. TAP was required in 93.3% of the patients. The median time of mechanical ventilation was 23.5 hours (range, 10 to 480 hours). Six patients (20%) required mechanical ventilation more than 48 hours. The median length of stay in the intensive care was 2 days (range, 2 to 20 days). The median duration of hospital stay was 9.5 days (range, 7 to 60 days). At follow-up 2-36 months later (median 12 months), there were no late deaths or reoperations. All except one were asymptomatic. Postoperative Echocardiography showed that right and left ventricular systolic functions were normal in all patients. The mean peak gradient across the RVOT was 26 ± 1.9 mmHg (range, 10 to 80 mmHg). All except 3 patients had free pulmonary regurgitation. Two patients (6.6%) required intervention in the form of balloon dilatation and stenting of left pulmonary artery in on patient and stenting of RVOT in the other.

Conclusions : This retrospective review demonstrates that early full repair of TOF in the first year of life is associated with an excellent survival and a low incidence of postoperative morbidity regardless of age, and the requirement for TAP.

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TOF was one of the first cyanotic congenital cardiac lesions to be treated with surgical intervention. Since the first Blalock-Taussig shunt in 1945, the philosophy of management of TOF has undergone considerable changes. With the development of cardiopulmonary bypass (CPB), full repair rather than palliation became the goal; however, total repair was deferred until later childhood. With increasing experience, improvements in CPB technique, and myocardial

protection, primary repair in infancy in symptomatic patients became common. (1-16) A major unresolved issue is the ideal timing for complete correction of patients with cyanotic tetralogy of Fallot (TOF). The arguments hinge on the morbidity and mortality of the operation. Young age, low weight, and the requirement for TAP reconstruction of the RVOT are thought to adversely affect the results of intracardiac repair of TOF. (4,6) The purpose of this retrospective study is to evaluate the current results of full repair of TOF in infancy. This study also would test the hypothesis that primary repair of TOF can be performed safely in symptomatic infants, regardless of age, weight or the use of TAP.

Methods

From October 2000, to July 2004, 74 patients with symptomatic TOF were operated at our hospital. All patients ≤ 12 months of age who underwent primary full repair of TOF were the subject of this study. Patients who had pulmonary atresia and those who underwent initial palliative shunt were excluded. Patients who had an associated atrial septal defect and/or patent ductus arteriosus were included in this study. Patients' records were reviewed retrospectively. Preoperative, operative, and postoperative data were reviewed. The immediate postoperative study included the following: Thirty-day mortality, arrhythmias, complete heart block, neurological complications, the requirement for open chest, the use of inotropic support, durations of mechanical ventilation, ICU stays and total hospital stays. Patients were followed until their last clinic visit. Late postoperative evaluation included a complete physical examination, an electrocardiogram and two-dimensional and Doppler ECHO in all patients. The 30-day mortality was defined as death within the first month postoperatively.

Operative Procedures : The operative technique was uniform throughout this study. Standard CPB with systemic hypothermia was instituted through an ascending aortic cannula and two venous cannulas with caval taping. After aortic cross-clamping, the myocardium was protected with topical hypothermia and cold blood cardioplegic solution was used in a dose of 20-30mL initially and 10-15mL/kg every 20-30 minutes. Before removal of the aortic-cross clamp a warm blood perfusion was given for 2-3 minutes. Conventional ultrafiltration was done during CPB in all patients and modified ultrafiltration was used according to surgeon preference. Operative repair was as follow: After initiation of CPB, a right atriotomy was performed and the atrial septum was inspected. Working through the tricuspid valve, a moderate resection of the parietal

and septal extensions of the infundibular septum was performed. The dissection was carried upward to the level of pulmonary annulus. Hegar dilators were passed through the tricuspid valve into the RVOT to estimate its size. If the annular diameter at this point was less than the mean normal diameter predicted by Rowlatt and colleagues (17), then the main pulmonary artery was incised. Additional subvalvar infundibular muscle was resected through the pulmonary valve if necessary. In order to relieve the obstruction at the annular level, while trying to preserve as much valvar function as possible, we utilized a technique of limited transannular patching. The longitudinal pulmonary arteriotomy was extended across the pulmonary annulus only as far as necessary, often only a few millimeters onto the infundibulum. In addition the transannular incision was performed through the commissure (usually the anterior), and exactly splitting it, and a very narrow elliptical pericardial patch was used to augment the annulus. The malalignment-type ventricular septal defect was closed with bovine pericardium using interrupted horizontal mattress sutures with Teflon pledgets. Ductus arteriosus and atrial septal defects were simultaneously closed. Temporary ventricular electrodes were placed in all patients.

Follow-up: Patients were followed until their last clinic visit. Late postoperative evaluation included a complete physical examination, an electrocardiogram and two-dimensional and Doppler ECHO in all patients.

Statistical Analysis : was performed using SPSS statistical program for windows (SPSS 11 Inc., Chicago, Illinois). Data are expressed as frequencies, medians with ranges and, means \pm standard deviation, as appropriate. A *P* value of ≤ 0.05 was considered significant.

Results

Preoperative Characteristics : - There were 30 patients met our inclusion criteria. Preoperative characteristics are shown in .

There were 20 boys and 10 girls. Their mean age at the time of the operation was 10.1 ± 2.1 months (range, 5 to 12 months). The mean body weight was 8.0 ± 2.3 kg, (range 4.5 to 16 kgs). One patient had a morbid obesity. Early repair was performed electively for hypoxic spells in 18 patients (60 %) and for persistent hypoxemia (Saturation $\leq 75\%$) in 6 patients (20%).

Six patients (20%) were operated on emergency/urgent basis due to severe desaturation during cardiac catheterization or multiple cyanotic spells. One patient had Trisomy 21.

Table I. Table I: Preoperative Data.

Variable	Results
Age (month)	10.1±2.1 (15-12)*
Weight (kg)	8.0±2.3 (4.5-16)*
BSA (m ²)	0.39±0.07 (0.27-0.65)*
Room air saturation (%)	77±16.7 (30-98)*
Preoperative hemoglobin (mg/L)	156±29 (109-230)*
Sex	
Male	20 (66.6%)**
Female	10 (33.3 %)**
History of cyanotic spells	18 (60 %)**
B-Blocker use	18 (60%)**
Trisomy 21	1 (3.3%)**
hypospadias	2 (6.6%)**

* Values are expressed as mean ± SD with the range in parentheses.

** Values are expressed as the number of the patients with the percentages in parentheses.

All patients underwent preoperative ECHO examination. The preoperative ECHO data are shown in Tables II and III.

Table II: Preoperative ECHO Data.

Variable	Mean	Range
Right ventricular outflow tract peak gradient (mmHg)	75.2±14	50-106
Pulmonary annulus size (mm)	6.7±2.1	2-12
Left pulmonary artery size (mm)	5.7±1.2	3-8.0
Right pulmonary artery size (mm)	5.8±1.3	4-9.0

Table III: Associated cardiovascular defects.

Defects	No. of patients (%)
Atrial septal defect	7 (23.3%)
Patent ductus arteriosus	3 (10%)
Right aortic arch	5 (16.6%)
Bilateral Superior vena cava	3 (10%)
LPA stenosis	2 (6.6%)
Coronary anomalous	2 (6.6%)
Situs inversus	1 (3.3%)
Aorto-pulmonary collaterals	
Significant	1 (3.3%)
Insignificant	2 (6.6%)

Apart from the typical features of TOF, the significant preoperative ECHO findings were associated atrial

septal defect in seven patients (23.3%) and patent ductus arteriosus in 3 patients (10%). Associated intrathoracic abnormalities were noted in 11 patients, including right aortic arch in 5 patients (16.6%), and bilateral superior vena cava in 3 patients (10%). Two patients (6.6%) had significant stenosis of the proximal portion of LPA. One patient had situs inversus. Preoperative cardiac catheterization was performed in 5 patients (16.6%) to clarify coronary artery anatomy, to better define the pulmonary artery anatomy, or to identify aortopulmonary collaterals. One patient had significant major aortopulmonary collaterals. Two patients had multiple insignificant aortopulmonary collaterals. Two patients had coronary artery abnormality in the form of left anterior descending from right coronary artery in one patient and a single coronary artery in the other.

Operative Characteristics : (Table IV) Mean CPB time for repair was 137±34 minutes, and the mean cross-clamp time was 107±29 minutes. The operative approach to close the VSD was through the right atrium in all patients. The RVOT was resected by the transatrial approach with additional resection through the pulmonary valve in all patients. A TAP was required in 28 patients (93.3%). Branch pulmonary arterioplasty was performed in 2 patients. In 3 patients, pop-off interatrial septal defects were left electively. No patients required placement of a right ventricle to pulmonary artery conduit as the patient with anomalous origin of the left anterior descending from the right coronary underwent a very limited ventriculotomy extension from the pulmonary annular incision which was sufficient to relieve the infundibular obstruction without injuring the left anterior descending artery. In two patients, the sternum was left open at the end of procedure because of tissue edema and low cardiac output postoperatively.

Table IV: Intraoperative data

Variable	Results
Cardiopulmonary bypass time(min)	137±34 (85-219)
Cross-clamp time(min)	107±29 (64-176)
Temperature C°	30(28-32)
Use of TAP	28(93.3%)
Pulmonary arterioplasty	2(6.6%)
Use of modified ultrafiltration	17(56.6%)
Open chest	2(6.6%)
Elective Pop-off interatrial septal defect	3(10%)

* Values are expressed as mean ± SD with the range in parentheses.

** Values are expressed as the number of the patients with the percentages in parentheses.

Postoperative characteristics:-

Early results: Tables V & VI show the early postoperative results. There were no deaths during the postoperative hospital stay. However, one patient (3.3%) died following discharge from the hospital, 25 days after surgical repair (15 days post discharge). It occurred in a 7-month old Down's syndrome infant who suffered from multiple cyanotic spells and operated urgently. He had an uncomplicated early postoperative course. Three days post discharge; he was readmitted with a picture of pericardial effusion.

Table V: Early postoperative results.

Variable	No. (%)
Thirty-day mortality	1 (3.3%)
Arrhythmias	
JET Treatment with amiodarone	3 (10%)
No treatment with amiodarone	12 (40%)
Peritoneal dialysis	1(3.3%)
Inotropes more than 48 hours	2(6.6%)
Neurological complications	0
Superficial wound infection	3 (10%)

Table VI: Early postoperative results.

Variable	Median	Range
Mechanical ventilation (hrs)	23.5	10-480
ICU Stay (days)	2	2-20
Total hospital stay (days)	9.5	7-60

ECHO showed that there was mild pericardial effusion with no signs of tamponade. The patient was discharged from our hospital in a stable condition. Ten days later he died in a local hospital, and his death is presumed to have been due to increasing pericardial effusion that led to cardiac tamponade. No patient developed a neurological deficit. Postoperative rhythm abnormalities included transient junctional ectopic tachycardia (JET) that occurred in 15 patients (50%). Of these patients only 3 patients showed signs of cardiovascular compromise and were treated with amiodarone. By the time of discharge all patients had reverted to a normal sinus rhythm. Two patients required high doses of inotropes for more than 48 hours. The median length of stay in the intensive care was 2 days (range, 2 to 20 days). The two patients who left the operating room with open

chest underwent delayed chest closure on postoperative day 2 and 3. The median time of mechanical ventilation was 23.5 hours (range, 10 to 480 hours). Six patients (20%) required mechanical ventilation more than 48 hours. Table VII shows the factors that led to prolonged mechanical ventilation which included open chest in two patients, low cardiac output with acute renal failure in one patient, acute respiratory distress syndrome which required high frequency ventilation in one patient, severe reactive airway disease in a morbid obese patient, and the last one had preoperative major aortopulmonary collaterals (MAPCA) and it was difficult to wean him off ventilator except after cardiac catheterization and coiling of the collaterals. The median duration of hospital stay was 9.5 days (range, 7 to 60 days). Nine patients required hospital stay more than 10 days.

Table VII: Causes of prolonged mechanical ventilation ≥ 48 hours

Variable	No. (%)
Open chest	2 (6.6%)
Low cardiac output	1 (3.3%)
Acute respiratory distress syndrome	1 (3.3%)
MAPCs	1 (3.3%)
Severe reactive airway	1 (3.3%)
Total	6 (20%)

Table VIII shows the factors that led to delayed discharge which included prolonged mechanical ventilation in the above mentioned 6 patients, repair of malrotation and gangrene in left foot secondary to femoral artery cannulation in one patient, postoperative fever with negative cultures in one patient, and repair of incisional hernia at the site of peritoneal dialysis wound in one patient. Three patients had superficial sternal wound infections that were treated conservatively.

Table VIII: Causes of prolonged hospital stay ≥ 10 days

Variable	No. (%)
Prolonged mechanical ventilation	6 (20%)
Malrotation & Gangrene	1 (3.3%)
Postoperative fever	1 (3.3%)
Repair of incisional hernia	1 (3.3%)
Insertion of a permanent pace maker	1 (3.3%)
Total	9 (3 %)

Late Results:- Tables IX shows the late post operative results. Two patients could not be traced for follow-up as a substantial portion of our patients are referred to our hospital from other areas (in and out of the Saudi Arabia). The median follow-up of the survivors was 12 months after surgery (range 2-36 months). There were no late deaths. There were no reoperations during the follow-up period.

Table IX: Postoperative late results

Variable	No. (%)
Late mortality	0
Rhythm	
SR	22 (73.3%)
SR with right bundle branch block	8 (26.6%)
Reoperation	0
Intervention	2 (6.6%)
Follow-up months	Median 12 (Range, 2-36)

All except one were asymptomatic. This patient was in congestive heart failure and responded well to intensive antifailure treatment. All patients were in normal sinus rhythm; a right bundle branch block pattern was present on electrocardiogram in 8 patients (26.6%). No patient was taking anti-arrhythmic drugs. Echocardiography was performed in all patients available for follow-up (Table X). At the time of most recent follow-up, Echocardiography showed that right and left ventricular systolic functions were normal in all patients. The mean peak gradient across the RVOT was 26 ± 1.9 mmHg (range, 10 to 80 mmHg). All except 3 patients had free pulmonary regurgitation. One patient had severe Tricuspid regurgitation and 3 patients had moderate regurgitation. Six patients had a trivial, hemodynamically insignificant residual interventricular communications. Two patients (6.6%) underwent balloon dilatation and stenting. One patient, 19 months after primary repair, had diffusely small LPA (4mm) and a peak gradient of 35 mmHg. He underwent balloon dilatation and stenting of the left pulmonary artery. Follow-up ECHO showed patient stent and pressure gradient decreased to 17 mmHg. The other patient, 24 months after primary repair, had residual stenosis starting below the pulmonary valve with a peak gradient of 80 mmHg and required stenting of RVOT and the peak gradient decreased to 35 mmHg.

Table X: Post operative ECHO results

Variable	Value
Peak RVOT gradient (mmHg)	26 ± 1.9 (10-80)
Free Pulmonary insufficiency	27 (90%)
Tricuspid insufficiency	
Severe	1 (3.3%)
Moderate	3 (10%)
Residual VSD	
Non significant	6 (20%)
Significant	0

Discussion

The traditional approach to the management of cyanotic infants with TOF has been initial shunt followed by a complete repair after the first 6 months of age. Improvements in cardiac anesthesia, cardiopulmonary (CPB) technology, better myocardial preservation, and postoperative intensive care have led to increasing trend to perform primary full repair in the first few months of life. The rationale for early primary repair is documented by several studies⁽¹⁻¹⁶⁾ and data favoring an early repair are increasing:

1. Rabinovitch and his colleagues⁽¹⁸⁾ demonstrated that early repair of TOF could result in a normal number of alveoli and normal growth of proximal and peripheral pulmonary arteries.
2. The distensibility and growth potential of the pulmonary arteries following repair is probably related in part to the elastin content of the pulmonary arteries. The ability to synthesize elastin is probably maximal during the neonatal period and early infancy.⁽¹⁹⁾
3. Biopsies from the right and the left ventricles showed an abnormal increase in the fibrous component with age in the right ventricles, and this may be the substrate for arrhythmias and ventricular dysfunction.⁽²⁰⁾
4. Electrophysiological studies by Ewing and colleagues⁽²¹⁾ showed that ventricular arrhythmias may be decreased with early repair of TOF.
5. The study of Castaneda and colleagues⁽²²⁾ showed that the right ventricular hypertrophy is probably induced by RVOT obstruction and increases with age.
6. Some studies⁽²³⁻²⁵⁾ demonstrated that ventricular arrhythmias are related to the timing of the operation rather than to the operation itself, and suggested that early operation may reduce the occurrence of late arrhythmias.
7. Borrow and colleagues⁽²⁶⁾ observed that early repair

of TOF may preserve left ventricular function especially with after-load stress using methoxamine.

In addition, initial aortopulmonary shunts are not without morbidity and mortality.^(27,28) Aortopulmonary shunts are associated with shunt obstruction/occlusion, pulmonary artery distortion, volume overload of the left ventricle, and the potential for the development of pulmonary vascular obstructive disease. However, proponents of a two-stage approach emphasize on low morbidity and mortality of an initial aortopulmonary shunt and the potential for growth of the pulmonary arteries, avoiding a subsequent TAP. Advocates of the traditional approach would also argue that complete repair in small infants may carry an increased mortality and morbidity compared to delayed repair at older age. Age, weight and TAP have been implicated as independent risk factors for early repair.^(4,6) In our study, we tried to clarify the role of these risk factors and we reviewed all patients less than 12 months who had undergone primary full repair of TOF in our hospital.

Effect of Age and Weight: The optimal age for TOF repair remain controversial. In the past, very young age had been considered as a risk factor for hospital mortality. Small size and immaturity of organs were believed to increase the vulnerability of the infant to the generalized insult of CPB or hypothermic arrest. However, in recent years, successful neonatal open heart surgery performed for a number of complex congenital anomalies encouraged the early repair of most congenital anomalies including TOF. This has been illustrated by Kirklin and colleagues⁽¹²⁾ by reviewing their experience between 1967 and 1986. They reported a higher mortality in the subgroup of patients with younger age at the time of repair. As their experience and knowledge had grown, the incremental risk of young age was not apparent until age is less than 3 months. The incremental risk of young age may be related to the inability of the young right ventricle to adjust to volume overload after full repair. In our study, there were an insufficient number of deaths to include this as an outcome. The 30-day mortality was low 3% (1 of 30) and no statistical inferences could be drawn. It worthwhile to mention that this death occurred as a result of a preventive cause (Pericardial effusion). A better close observation of this patient would have prevented his death. Our results are consistent with other studies⁽¹⁻¹⁶⁾ and suggesting that primary repair of TOF can be performed with a low mortality. The reduction of age at which risk is increased is no doubt, in part, the result of the increasing technical experience in intracardiac surgery and the early post operative care in the very young. On the other hand, older age at repair was

a risk factor for mortality early and late after repair.⁽¹⁶⁻²⁹⁾ Van Arsdell and his colleagues,⁽¹⁶⁾ in an effort to define the optimal age for repair of TOF, reported their experience with 227 patients. The median age of repair was 14 months (range, 8 days to 9.6 years). They observed that the best survival and physiological outcomes were achieved with primary repair in children aged 3 to 11 months. Multivariate analysis demonstrated that an age less than 3 months was independently associated with increase morbidity but not mortality, and age more than 11 months was associated with increased mortality. Supporting this observation, Van Dongen and his colleagues⁽²⁹⁾ has found that age less than 3 months was associated with increased use of inotropic support, a higher incidence of organ dysfunction and a prolonged ventilator support. Murphy and his colleagues⁽³⁰⁾ also reported that mortality was related to older age at the time of repair (more than two years). This may be due to irreversible effect of long standing RV hypertrophy, cyanosis and polycythemia on cardiac structure and function. Gatzoulis and colleagues⁽³¹⁾ reported that RV hypertrophy begin shortly after birth, continues as age increases, and begin to be irreversible by 4 year of age. This hypertrophy often requires extensive muscular resection, which may form a potential substrate for ventricular arrhythmias and dysfunction.

TAP and Mortality: There is a general acceptance that an early approach to full repair of cyanotic TOF will be associated with a perceived increase in the need for TAP that would result in damaging the pulmonary valve.^(9,32) This latter observation, however, does not appear logical for two reasons. First, the RVOT is unlikely to grow, as there is reduced flow through it. Second, the data reported from several studies,⁽³⁻⁶⁾ repair was performed in severely symptomatic infants; infants with the worst anatomy (very small pulmonary annuli) were selected out to undergo surgery. In our study, all except two required TAP and this is in accordance other series^(14,33) which showed incidences between 85% and 90%. The high incidence of TAP is reflective of the selection process for surgery rather than being intrinsic to young age as 40% of our patients were operated on emergency basis and/or for persistent hypoxemia reflecting worse anatomy.

TAP was observed to increase operative mortality as reported by Hammon and colleagues.⁽⁶⁾ TAP increased operative mortality to 15.8% in infants compared with 0% in older children without TAP. Kirklin and colleagues⁽⁴⁾ also reported that TAP was an independent incremental risk factor for mortality following primary repair of TOF.

The freedom from reoperation: in our series is excellent (0%). Only two patients (6.6%) required intervention during the follow-up period. In one patient, 24 months after primary repair, residual stenosis starting below the pulmonary valve was found and required stenting of RVOT. This may be related to our technique that includes non-aggressive resection of the RVOT muscles to prevent weakness of the right ventricular wall. In the other patient, 19 months after primary repair, a diffusely small LPA (4mm) was found and required balloon dilatation and stenting of the left pulmonary artery. Residual obstructions that include LPA origin were observed in some studies.^(43,44) Ductal tissues have been reported to extend into this area. Constriction and fibrosis of this ductal tissue after the neonatal period (and hence after repair) may explain this stenosis. Extension of pericardial patch across LPA origin would have avoided this problem.

It was anticipated that there might be a clinically important increase in early postoperative morbidity associated with early repair of TOF. This is might be reflected in an increased duration of mechanical ventilation, hemodynamic support and a higher incidence of organ system failures. However, this concern was not observed in our study. Given that all patients who undergo repair of congenital heart disease will develop a certain degree of cardiorespiratory impairment, it is worth noting that only six patients (20%) of our patients required mechanical ventilation \geq 48 hours. Two of them had preoperative comorbidity. One patient, with a morbid obesity, had a preoperative severe reactive airway in one patient. The other patient had associated MAPCs that led to flooding of the lungs and difficulty in extubation. This patient was extubated early after coiling of the MAPCs. This resulted in increased length of ICU stay, but there was no effect on short-term morbidity.

Although the number of patients in our study is small and the follow-up is still short, this study shed some lights on the effect of young age and the requirement for TAP on the outcome the surgical repair of TOF in infancy. A longer follow-up is needed for this group of patients to assess the long-term results of early repair of TOF.

Conclusion

This retrospective review demonstrates that early repair of TOF is associated with excellent survival and a low incidence of postoperative morbidity. Early definitive repair in severely cyanotic TOF is associated with an increased requirement for TAP but it did not have an impact on operative mortality or morbidity.

References

1. Barratt-Boyes B and Neutze J. Primary repair of tetralogy of Fallot in infancy using profound hypothermia with circulatory arrest and limited cardiopulmonary bypass. *Ann Surg* 1973; 178: 406-411.
2. Starr A, Bonchek L, and Sunderland C. Total correction of tetralogy of Fallot in infancy. *Thorac Cardiovasc Surg* 1973; 65: 45-57.
3. Tucker W, Turley K, Ullyot D, et al. Management of symptomatic tetralogy of Fallot in the first year of life. *J Thorac Cardiovasc Surg* 1979; 78: 494-501.
4. Kirklin J, Blakstone E, Pacifico A, et al. Routine primary repair vs. two stage repair of tetralogy of Fallot. *Circulation* 1979; 60: 373-379.
5. Kirklin JW, Blakstone E, Kirklin JK, et al. Surgical results and protocols in the spectrum of tetralogy of Fallot. *Ann Surg* 1983; 198: 251-265.
6. Hammon J, Henry C, Merrill W, et al. Tetralogy of Fallot: Selective surgical management can minimize operative mortality. *Ann Thorac Surg* 1985; 40: 280-284.
7. Zhao H, Miller D, Reitz B, et al. Surgical repair of tetralogy of Fallot. *J Thorac Cardiovasc Surg* 1985; 89: 204-220.
8. Kirklin J, Blackstone E, Colvin E, et al. Early primary correction of tetralogy of Fallot. *Ann Thorac Surg* 1988; 45: 231-233.
9. Gustafson R, Murray G, Warden H, et al. Early primary repair of tetralogy of Fallot. *Ann Thorac Surg* 1988; 45: 235-241.
10. Touati G, Vouche P, Amodeo A, et al. Primary repair of tetralogy of Fallot in infancy. *J Thorac Cardiovasc Surg* 1990; 99: 396-403.
11. Groh M, Melions J, Bove E, et al. Repair of tetralogy of Fallot in infancy: effect of pulmonary artery outcome. *Circulation* 1991; 84(Supp) III 206-212.
12. Kirklin J, Blakstone E, Joans R, et al. Morphological and surgical determinants of outcome after repair of tetralogy of Fallot and pulmonary stenosis: A two-institutional study. *J Thorac Cardiovasc Surg* 1992; 103: 706-723.
13. Uva M, Chardigny C, Galetti L et al. Surgery for tetralogy of Fallot at less than six months of age. *J Thorac Cardiovasc Surg* 1994; 107: 1291-1300.
14. Caspi J, Zalstein E, Zucker N, et al. Surgical management of tetralogy of Fallot in the first year of life. *Ann Thorac Surg* 1999; 68: 1344-1349.
15. Pigula F, Khalil P Mayer J. et al. Repair of tetralogy of Fallot in neonate and young infants. *Circulation* 1999; 100(Supp) II 157-161.
16. Van Arsdell G, Maharaj G, Tom J, et al. What is the optimal age of repair of tetralogy of Fallot? *Circulation* 2000; 102(Suppl III): III 123-129.
17. Rowlatt J, Rimoldi H, and Lev M. The quantitative anatomy of the normal child's heart. *Pediatr Clin North Am* 1963; 10: 499-587.
18. Rabinovitch M, Herrera-Deleon V, Castaneda A, et al. Growth and development of the pulmonary vascular bed in patients with tetralogy of Fallot with or without pulmonary atresia. *Circulation* 1987; 94: 498-503.

19. Rosenberg H, Williams W, Trusler G, et al. Structural composition of central pulmonary arteries. *J Thorac Cardiovasc Surg* 1985; 89: 204-220.
20. Hegerty A, Anderson R, and Deanfield J. Myocardial fibrosis in tetralogy of Fallot: effect of repair or part of natural history? *J Am Coll Cardiol* 1988; 11: 138A.
21. Ewing L, Gillette E, Zeigler V, et al. Only 8 % of post-operative tetralogy patients have inducible ventricular arrhythmias. *J Am Coll Cardiol* 1987; 9: 38A.
22. Castaneda A, Freed M, Williams R, et al. Repair of tetralogy of Fallot in infancy. *J Thorac and Cardiovasc Surg* 1977; 74: 372-381.
23. Deanfield J, Mc Kenna W, Presbitero P, et al. Ventricular arrhythmias in unrepaired and repaired tetralogy of Fallot: relation of age, timing of repair, and hemodynamic status. *Br Heart J* 1984; 52: 77-81.
24. Sullivan I, Presbitero P, Gooch V, et al. Is ventricular arrhythmia in repaired tetralogy of Fallot an effect of operation or a consequence of the course of the disease? A prospective study. *Br Heart J* 1987; 58: 40-44.
25. Kobayashi J, Hirose H, Nakano S, et al. Ambulatory electrocardiographic study of the frequency and the cause of ventricular arrhythmia after correction of tetralogy of Fallot. *Am J Cardiol* 1984; 54: 1310-1313.
26. Borrow K, Green L, Castaneda A, et al. Left ventricular function after repair of tetralogy of Fallot and its relationship to age at surgery. *Circulation* 1980; 61: 1150-1158.
27. Barbosa R, Somerville J, and Ross D. Aorto-right pulmonary artery anastomosis: long-term problems and results after correction. *Am J Cardiol* 1974; 33: 125-131.
28. Greenwood R, Nadas A, Rosenthal A, et al. Ascending aorto-pulmonary artery anastomosis for cyanotic congenital heart disease. *Am Heart J* 1977; 14: 94-99.
29. Van Dongen E, Glansdorp A, Mildner R, et al. The influence of perioperative factors on outcomes in children aged less than 18 months after repair of tetralogy of Fallot. *J Thorac and Cardiovasc Surg* 2003; 126: 703-710.
30. Murphy J, Gersh B, Mair D, et al. Long term outcome in patients undergoing surgical repair of tetralogy of Fallot. *N Eng J Med* 1993; 329: 593-599.
31. Gatzoulis M, Balaji S, Webber S, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot. *Lancet* 2000; 356: 975-981.
32. Hennein H, Mosca R, Urcelay G, et al. Intermediate results after complete repair of tetralogy of Fallot in infants. *J Thorac and Cardiovasc Surg* 1995; 109:332-344.
33. Kaushal S, Iyer K, Sharma R, et al. Surgical experience with total correction of tetralogy of Fallot in infancy (Abstract). *Inter J Cardio* 1996; 56: 35-40.
34. Ellison R, Brown W, Yeh T, et al. The significance of acute and chronic pulmonary valvular insufficiency. *J Thorac Cardiovasc Surg* 1970; 60: 549-551.
35. Calder A, Barratt-Boyes B, Brandt P, et al. Postoperative evaluation of patients with tetralogy of Fallot repaired in infancy. *J Thorac Cardiovasc Surg* 1980; 77: 701-709.
36. Murphy J, Freed M, Keane J, et al. Hemodynamic results after intracardiac repair of tetralogy of Fallot. *Circulation* 1980; 62: (Suppl I) 168-172.
37. Walsh E, Rockenmacher S, Keane J, et al. Late results in patients with tetralogy of Fallot repaired during infancy. *Circulation* 1988; 77: 1062-1067.
38. Oku H, Shirotani H, Sunakawa A, et al. Postoperative long-term results in total correction of tetralogy of Fallot: hemodynamic and cardiac function. *Ann Thorac Surg*; 1986; 41: 413-419.
39. Zahka K, Horneffler P, Rowe S, et al. Long-term valvular function after total repair of tetralogy of Fallot: relation to ventricular arrhythmias. *Circulation* 1988; 78 :(Suppl III) 14-23.
40. Katz N, Blackstone E, Kirklin J, et al. Late survival and symptoms after repair of tetralogy of Fallot. *Circulation* 1982; 65: 403-410.
41. Chandar J, Wolf G, Garson A, et al. Ventricular arrhythmias in postoperative tetralogy of Fallot. *Am J Cardiol* 1990; 65: 55-61.
42. Rouillard K, Hanley F and Dorostakar P. Early repair of tetralogy of Fallot is associated with a higher incidence of postoperative junctional ectopic tachycardia. (abstract). *J Am Coll Cardiol* 1998; 355.
43. Di Donato R, Joans R, Lang P, et al. Neonatal repair of tetralogy of Fallot with and without pulmonary atresia. *Thorac Cardiovasc Surg* 1991; 101: 126-137.
44. Elzenga N, and Gittenberger-de Groot A. The ductus arteriosus and stenosis of the pulmonary arteries in pulmonary atresia.(Abstract). *Int J Cardiol* 1986;11: 195-208.