

**SREE CHITRA TIRUNAL INSTITUTE FOR  
MEDICAL SCIENCES AND TECHNOLOGY  
THIRUVANANTHAPURAM**

**DEPARTMENT OF CARDIOLOGY**



**ARRHYTHMIAS IN POST SURGICAL TETRALOGY OF  
FALLOT PATIENTS**

**A THESIS SUBMITTED FOR THE DEGREE OF**

**DM CARDIOLOGY**

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**JANUARY 2021**



**DEPARTMENT OF CARDIOLOGY,  
SCTIMST, TRIVANDRUM  
CERTIFICATE**

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I hereby certify that the work in this dissertation titled “Arrhythmias in Post-Surgical Tetralogy of Fallot Patients” is a certified record of original research work undertaken by Dr. Karthik R in the Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology in partial fulfilment of requirement for the award of D.M. Cardiology degree.

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**DECLARATION BY CANDIDATE**

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I, Dr.Karthik R, hereby declare that the project in this book, titled “Arrhythmias in Post-Surgical Tetralogy of Fallot Patients” was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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## DEPARTMENT OF CARDIOLOGY SCTIMST, TRIVANDRUM

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# **TITLE**

## ***“ARRHYTHMIAS IN POST SURGICAL TETRALOGY OF FALLOT PATIENTS”***

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**Dr. Karthik R**

## ABBREVIATIONS

ToF	-	Tetralogy of Fallot
NYHA	-	New York Heart Association
ICR	-	Intracardiac Repair
TAP	-	Transannular Patch
RV	-	Right Ventricle
RVOT	-	Right Ventricular Outflow Patch
VSD	-	Ventricular Septal Defect
PA	-	Pulmonary artery
MR	-	Mitral regurgitation
PAH	-	Pulmonary artery hypertension
LA	-	Left atrium
RA	-	Right atrium
SD	-	Standard deviation
IQR	-	Interquartile range
RBBB	-	Right Bundle Branch Block
LAD	-	Left axis regurgitation
QRSd	-	QRS duration
cQT	-	Corrected QT interval
PLAX	-	Parasternal long axis view
PR	-	Pulmonary regurgitation

TR	-	Tricuspid regurgitation
EF	-	Ejection fraction
RVSP	-	Right ventricular systolic pressure
PASP	-	Pulmonary artery systolic pressure
CMRI	-	Cardiac Magnetic Resonance imaging
RVEDVI	-	Right ventricular End Diastolic Volume Index
RVESVI	-	Right ventricular End Systolic Volume Index
LGE	-	Late Gadolinium Enhancement



# **SYNOPSIS**

## **Background**

Tetralogy of Fallot (ToF) is the most common cyanotic congenital heart disease (0.34/1000 live births), with a good outcome after surgical correction. Arrhythmias are a common cause of morbidity and mortality in post-surgical ToF patients.

## **Aim**

To describe the arrhythmic complications in post-surgical ToF patients.

## **Methods**

This is a descriptive single-center study with retrospective case enrolment and cross-sectional follow-up. Patients who underwent surgical correction for ToF from January 1999 to December 2005 were identified by a search of an institutional database. All patients on follow-up were contacted by telephone. Clinical characteristics were noted and an electrocardiogram, 2D echocardiography, and 24-hour Holter study were done and analysed.

## **Results**

A total of 504 patients underwent surgical repair for ToF between January 1999 and December 2005. The median age at the time of surgery was 5(3-9) years and 57.9% were males. The most common surgical technique used was intracardiac repair and transannular patch [363(72.1%)]. 225(45.04%) of patients were on regular follow up. Most patients (83.6%) were asymptomatic (NYHA Functional Class I). The median QRS duration was 130 (120-150) ms and right bundle branch block was noted in 71.1% of patients. Arrhythmias were documented in 25.7% of patients in ECG and on 27.4% of patients on 24-hour Holter and all arrhythmias increased with a longer duration of follow up. Ventricular arrhythmias were the most common form of arrhythmias in ECG and 24-hour Holter (11.4% and 17.6%). Right ventricular dilatation (2D PLAX) and dysfunction on follow-up were independently associated with the development of atrial arrhythmias. The presence of right bundle branch block with left axis deviation (RBBB+LAD) and prolonged PR interval was independently associated with the

development of bradyarrhythmias on follow up. Kaplan Meier analysis of arrhythmias on follow up show an increase in incidence of arrhythmias with longer duration of follow up.

### **Conclusion**

Arrhythmias in post-surgical Tetralogy of Fallot patients were documented in the electrocardiogram and 24-hour Holter in 1/4<sup>th</sup> of patients with ventricular arrhythmias being more common on follow up. The presence of right ventricular dilatation and dysfunction were independently associated with development of atrial arrhythmias. The incidence of all arrhythmias increased with a longer duration of follow up.



# INTRODUCTION

Tetralogy of Fallot (ToF) is the most common type of cyanotic congenital heart disease with an incidence of 0.34 per 1000 live births(1). The first surgical correction for ToF was performed in the year 1954(2). Since then, multiple epidemiological studies have collected evidence regarding the natural history of patients who have undergone surgical correction for ToF and revealed that these patients have a 30-year survival rate of around 90%(3).

Arrhythmias in post-surgical ToF patients are an important cause for morbidity and mortality on long term follow up. On further analysis of the survival curves of these patients, it was noted that late mortality increases postoperatively beyond 25 years from 0.24%/year to 0.94%/yr. The main cause of this late mortality was sudden cardiac death due to sustained ventricular tachycardia or ventricular fibrillation(4).

Arrhythmias in these patients occur due to electrical instability secondary to anatomical modifications after surgery or from mechanical causes such as ventricular dilatation or dysfunction. The fibrous tissue that forms around the surgical scar can form a substrate for reentrant arrhythmias. Local abnormalities in ventricular depolarization and repolarization are also responsible for the genesis of cardiac arrhythmias(5).

In view of the increasing number of patients with surgical correction of ToF surviving into adulthood, the complete understanding of the risk factors for the development of arrhythmias is of paramount importance to identify a subgroup of patients who will require monitoring and further management.

Sree Chitra Tirunal Institute of Medical Sciences and Technology (SCTIMST) is a tertiary care cardiac center located in Thiruvananthapuram, Kerala. It caters to patients from Kerala and the border districts of Tamil Nadu. There is a large cohort of ToF patients who have undergone surgical correction in our Institute. We aim to describe the arrhythmic complications in patients with surgical correction of ToF and examine the risk factors that predispose to the development of arrhythmias.



# **REVIEW OF LITERATURE**

Tetralogy of Fallot (ToF) was first described in the year 1888 by Louis Arthur Etienne Fallot. He termed the condition as La Maladie Bleue and noted that the clinical description of this physiology was due to the combination of anatomic malformations, now referred to as tetralogy of Fallot(6). The combination included the presence of a ventricular septal defect, a biventricular connection of the aortic root which overrides the ventricular septum, right ventricular outflow tract obstruction, and right ventricular hypertrophy(7).

ToF is the most common type of cyanotic congenital heart disease with an incidence of 0.34 per 1000 live births(1). Surgical correction of this condition can be done with good outcomes with a survival rate at 30 years being 90%(3).

The surgical technique for the correction of ToF has undergone various improvements since the first ToF surgery in 1955. This is mainly due to the variability of phenotypic presentation of the condition. The different approaches are tailored to patients' anatomy with special consideration given to the right ventricular outflow tract and the related pulmonary valve stenosis.

The most common technique of repair in the initial surgeries was ventricular septal defect closure and transannular right ventricular (RV) outflow patch to relieve the obstruction. However, this is not to be considered as a complete resolution of the disease as it treats the problem of cyanosis, but the patient will require subsequent interventions to treat the surgical sequelae. The most commonly used surgical strategy presently is based on the concept that the pulmonary annulus may be preserved and a mixed lesion of moderate pulmonary stenosis and associated regurgitation has better outcomes than relief of the obstruction and free pulmonary regurgitation. On follow up the transannular patch results in free pulmonary regurgitation and the pulmonary stenosis that remains after the conservative surgical approach leads to RV dilatation and RV hypertrophy respectively(8).

### **Arrhythmias in post-surgical Tetralogy of Fallot**

The first surgical repair for ToF was performed by Dr. D.C.Lillehei in 1954. Around 15 to 20 years later the first cases of sudden cardiac arrest in surgically repaired ToF patients were noted and these were suspected to be due to malignant ventricular arrhythmias(9). Since then, sudden cardiac death has been reported repeatedly as the major cause of death in repaired ToF. Many studies have assessed the risk of sudden cardiac death in TOF and noted it to be between 0-0.8% yearly(10,11). Analysis of survival curves shows that these patients have a late mortality increases postoperatively beyond 25 years from 0.24% per year to 0.94% per year(4).

### **Mechanisms of Arrhythmias**

Arrhythmias occur in post-surgical ToF patients due to multiple reasons. The sequelae of the initial surgery which includes scar formation leads to the development of reentrant circuits(12). The formation of these circuits requires a region of slow conduction that is usually bordered by the electrically unexcitable scar tissue that is pathognomonic of a ventriculotomy scar or patch material(13).

Increasing severity of pulmonary regurgitation results in chronic right ventricular volume overload, right ventricular dilatation and QRS prolongation. Gatzoulis et al studied the mechano-electrical factors in 178 post-surgical ToF patients and noted that a QRS duration of 180 milliseconds or longer was predictive of life-threatening ventricular tachycardia with a sensitivity of 100% and specificity of 96%(14).

The mechanism for the development of atrial tachycardia is due to hemodynamic factors. In studies that used animal models to reproduce the different hemodynamic conditions following ToF repair, it was noted that those animals with chronic right ventricular(RV) volume overload due to pulmonary valvotomy were significantly more likely to develop sustained atrial arrhythmias(15).

Post-surgical ToF patients who develop atrial tachycardia have been reported to have significantly larger mean right atrial dimensions and volume compared to age-match patients without arrhythmias (16). Assessment of RV diastolic function by tissue doppler imaging has shown that reduced early RV diastolic velocity is significantly reduced in post-surgical ToF patients that develop atrial arrhythmias(17).

Despite the presence of a scar due to the previous atriotomy, Mah et al noted that the most frequently observed atrial tachycardia in these patients is isthmus-dependent atrial flutter and the cavotricuspid isthmus has been identified as the critical area for ablation in most patients(18). They also noted that 10% of patients with atrial arrhythmias were identified as focal atrial tachycardia. Chronic volume overload of the right atrium results in dilatation of the right atrium and in conjunction with an atriotomy incision leads to the development of scarring and fibrosis of the atrium resulting in the formation of micro-reentrant focal tachycardia(19).

### **Ventricular arrhythmias in post-surgical Tetralogy of Fallot**

Patients with a history of surgical repair for ToF have a high ventricular arrhythmia burden. Khairy et al studied 556 post-surgical ToF patients with a mean age of  $36.8 \pm 12$  years and followed up for 30 years post-surgery. They noted that 43.3% had documented atrial or ventricular arrhythmias. The most common subtype of arrhythmias documented in their study was ventricular tachycardia which was noted in 14.2% of patients. This was followed by intra-atrial re-entrant tachycardia (IART) in 11.5% of patients(20). Nakazawa et al studied arrhythmias late after repair in 512 post-surgical ToF patients with a mean follow-up duration of 11.7 years and noted that the incidence of ventricular arrhythmias was 3.5% with ventricular tachycardia occurring in 0.3% of patients(21). The difference between the incidence of ventricular arrhythmias between these two studies is likely due to the longer duration of follow-up and more advanced age of the patients in the former group.

The incidence of ventricular arrhythmias also depends on the route of surgical repair. Patients who underwent transatrial repair are less likely to develop ventricular arrhythmias. Dietl et al studied the incidence of arrhythmias in 2 groups of patients who underwent transventricular (n=71) or transatrial (n=36) repair. They noted that in the group that underwent transventricular repair, 39.4% of patients had significant ventricular arrhythmias while in the group that underwent transatrial repair only 2.8% of patients had significant ventricular arrhythmias(22).

Sudden cardiac death has been reported in 1.5-5% of patients after surgical repair of ToF and many studies have implicated ventricular arrhythmias as the causative factor(23,24). Garson et al studied 488 post-surgical ToF patients with a mean follow-up period of 6.1 years and noted that 13.5% of patients had ventricular arrhythmias on a routine electrocardiogram. Ventricular arrhythmias on routine electrocardiogram were noted in all patients who died of sudden cardiac death compared to 10% of patients who survived ( $p < 0.01$ ).

However, the incidence of sudden death depends on the duration of follow-up, with the incidence increasing with increasing duration of follow-up. Nollert et al studied 490 patients with ToF and noted that annual mortality increased from 0.24% per year to 0.94% after 25 years. They noted that the most common cause of death was sudden cardiac death(2.6%). They also found that higher age at surgery, elevated right ventricular systolic pressure postoperatively and preoperative polycythemia were risk factors for sudden cardiac death(4).

### **Electrocardiographic predictors of ventricular arrhythmias**

After surgical repair for ToF, the intraventricular conduction is prolonged and is indicated by the presence of a right bundle branch block. The right bundle branch block(RBBB) occurs commonly due to damage of the proximal right bundle during infundibular resection at the time of surgical repair(25). Incidence of right bundle branch block varies from 60% to 100% in this group of patients(26).

QRS duration has been found to have a significant correlation with the occurrence of ventricular arrhythmias. Gatzoulis et al studied the risk factors for arrhythmia and sudden cardiac death in 793 patients with surgical repair for ToF at a mean time of 21.1 years from surgery and noted that QRS duration was significantly higher in patients who developed ventricular tachycardia and in those who had sudden cardiac death(27).

A QRS duration  $>180$  ms has a 100% sensitivity for sustained ventricular tachycardia and sudden cardiac death, whereas a QRS duration of  $<180$ ms has a negative predictive value of 100% for these events(14). A high rate of increase in QRS duration(3.5ms/yr) has also been found to identify patients at risk of ventricular tachycardia and sudden

cardiac death(27). Balaji et al studied whether QRS duration can predict inducible ventricular tachycardia during an electrophysiological study in 135 patients of post-surgical ToF and noted that a QRS duration of >180ms had a high specificity for predicting ventricular tachycardia(28). Pulmonary regurgitation and right ventricular dilatation are associated with a prolonged QRS and these factors are also found to be significantly associated with sudden cardiac death(29).

Fragmented QRS complexes on ECG are associated with right ventricular dysfunction and myocardial fibrosis in post-surgical ToF patients(30,31). Egbe et al studied the role of QRS fragmentation for risk stratification in 465 adults who underwent surgical repair for ToF with a mean follow-up duration of 13.6 years. They noted that 12 % of patients had sudden cardiac death on follow up and the presence of a severe QRS fragmentation (involving  $\geq 5$  leads) and this was an independent predictor of all-cause mortality(32).

The corrected QT interval (QTc) is significantly associated with the development of ventricular tachycardia. Berul et al studied the electrocardiographic markers of late sudden death risk in 101 post-operative ToF patients with a mean follow-up duration of  $8.3 \pm 4.4$  years and noted 13.8% of these patients developed ventricular arrhythmias. They compared these patients to a control group of 1000 age and gender-matched subjects. The mean QTc in the control group was  $0.42 \pm 0.02$  seconds and  $0.53 \pm 0.05$  seconds in the ToF VT group which was statistically significant( $p < 0.01$ ). However, the authors concluded that when QRS prolongation and QTc were compared, a prolonged QRS duration had more sensitivity and specificity for identifying vulnerability to late-onset ventricular arrhythmias and sudden cardiac death(33).

### **Supraventricular Arrhythmias**

Adults with surgically repaired ToF develop increased right atrial pressure, hypertrophy, and fibrosis secondary to increased right ventricular end-diastolic pressure and chronic right ventricular systolic pressure overload resulting from pulmonary valve regurgitation. These hemodynamic changes in combination with the presence of an atriotomy scar leads to the development of atrial arrhythmias which are commonly re-entrant atrial tachycardias around the atriotomy scar(34).

Roos- Hesselink et al studied 53 patients with a mean age of 23.2 years who had undergone surgical repair of ToF at a mean age of 9.1 years and followed up for a mean duration of 17.5 years. They noted that 22.6 % of patients developed atrial fibrillation or flutter and 11.3 % of patients developed other forms of supraventricular tachycardia. It was also noted that atrial fibrillation or flutter occurred more commonly in patients who were older on follow up (35).

Another study by Harrison et al analyzed the atrial arrhythmias in 242 adults after surgical repair of ToF and noted that 12% of patients had atrial tachycardia. They compared the baseline characteristics and clinical outcomes of the group with atrial tachycardia with the remaining patients (arrhythmia free group). The authors noted that the group with atrial tachycardia had significantly more events (congestive cardiac failure, reoperation, subsequent ventricular tachycardia, stroke, and death) than the arrhythmia free group (69% vs 30%). The event-free survival was significantly lower in the atrial tachycardia group ( $18 \pm 2$  years vs  $28 \pm 16$  years,  $p < 0.001$ ). The atrial tachycardia group had a higher proportion of significant pulmonary regurgitation and mean right atrial volume than controls(36).

A multicenter study by Gatzoulis et al analyzed 793 post-surgical ToF patients with a mean age of 8.2 years and a mean follow-up duration of 21.1 years. They noted that 3.5% of the study population developed atrial flutter or fibrillation. A higher risk of sudden cardiac death and atrial arrhythmias were noted in patients with a greater age at the time of repair. The authors also noted that tricuspid regurgitation was the main risk factor for the development of atrial arrhythmias(27).

### **Bradyarrhythmias**

Post-surgical ToF patients are commonly found to have disturbances in atrioventricular conduction. This disturbance is usually indicated by the presence of a right bundle branch block (RBBB) which is seen in 80% of patients. Other patterns include a combination of right bundle branch block and left axis deviation in 11% of patients and combined right bundle branch block, left axis, and first degree atrioventricular (AV) block in 3% of patients. Most patients with RBBB after ventriculotomy have a benign prognosis(34).

A study by Garson et al analyzed 488 patients with a history of surgical repair for ToF with a mean age of repair of 6.4 years and a mean follow-up duration of 12.4 years. They noted complete right ventricular bundle branch block and left anterior hemiblock in 10.6% of patients. There were no patients with 2<sup>nd</sup> or 3<sup>rd</sup> degree AV block on routine electrocardiogram on follow up. In 2% of patients who underwent 24-hour holter on follow up short episodes of type I second degree AV block were noted (37).

A multicenter study conducted by Nakazawa et analyzed 512 patients post-surgical ToF patients with a mean age at surgery  $4.4 \pm 6$  years, mean age after follow up  $23.4 \pm 9.3$  years, and mean follow-up duration of  $11.7 \pm 7.2$  years. The prevalence of bradyarrhythmias in the study population was 8% and the incidence of 2<sup>nd</sup> and 3<sup>rd</sup> degree AV block were around 4% and 3% respectively. On analyzing patients with 3<sup>rd</sup> degree AV block they noted that majority of these patients had a perimembranous ventricular septal defect. The authors also noted that none of the patients who had perioperative transient complete AV block developed complete heart block on follow up. On follow-up, two patients with 2<sup>nd</sup> degree AV block progressed to complete heart block on follow up and required pacemaker implantation(21).

### **Ambulatory Holter Monitoring**

Ambulatory ECG (24-hour Holter) Monitoring has allowed for greater detection of supraventricular arrhythmias, ventricular ectopics, and non-sustained ventricular tachycardia. A study analyzing the outcomes of patients after surgical repair of ToF (with specific reference to the treatment of ventricular arrhythmias) in 488 patients with a mean follow-up of 7.3 years, noted that premature ventricular complexes were present in 13.7% of patients on a routine electrocardiogram. Only 97 patients had a 24 hour Holter done which showed ventricular arrhythmias in 73% of these patients. Premature ventricular complexes were noted in 56% of these patients and 6% of patients had ventricular tachycardia(37). The premature ventricular complex (PVC) rate ( $>10$  PVCs per hour ) detected on 24 hour Holter was noted in this study as a significant predictor of sudden cardiac death in post-surgical ToF patients and the authors noted that the reduction in PVC rate to  $<10$  PVC per hour reduces the rate of sudden cardiac death(37).

Cullen et al studied the prognostic significance of ventricular arrhythmia after repair of ToF in 86 patients with a follow-up duration of 12 years. Supraventricular arrhythmias were noted in 10.4% of patients. Patients were divided into two groups at the initial assessment based grade of ventricular arrhythmias on a 48 hour Holter (according to Lown criteria). The group that was classified as high grade of ventricular arrhythmias had 34.8% of patients with complex extrasystoles and 8.1% of patients had non-sustained ventricular tachycardia on 48 hour Holter. At the end of follow-up duration, the absolute difference in mortality between the two groups was 1.5% which was not found to be statistically significant(38).

A serial follow-up of adults with repaired tetralogy of Fallot was studied by Waijen et al in 151 patients with a mean follow-up duration of 3.2 years. A subgroup of 36 patients was followed up for a mean duration of 6.7 years with 3 yearly 24 hour Holter, exercise ECG and exercise radionuclide angiography. They noted that the overall mortality rate was low and clinically 94% of patients with New York Heart Association (NYHA) Functional Class I. Most patients in this study had no significant arrhythmias and no significant change in the severity of arrhythmias on follow up(39).

### **Echocardiographic Assessment**

After the surgical repair for ToF, one of the most important risk factors that determine both the right and left ventricular performance is pulmonary valve regurgitation(PR) (8). Depending on the severity of PR, there is progressive right ventricular dilatation and dysfunction. The dilatation of the tricuspid annulus due to chronic RV volume overload results in some degree of tricuspid regurgitation. Tricuspid regurgitation and right ventricular dilatation are important risk factors for the development of arrhythmias and sudden cardiac death(27).

The right ventricular dilatation and remodeling are secondary to volume and pressure overload cause alteration in the left ventricular and septal geometry. This along with post-surgical paradoxical septal motion and ventricular dyssynchrony result in left ventricular dysfunction(40).

The echocardiographic assessment of adult post-surgical ToF patients should be focused on the assessment of markers of right ventricular function and severity of pulmonary regurgitation in order to determine the appropriate timing for pulmonary valve replacement(41). The assessment of the RV after ToF surgery with echocardiography should include dimensional measurements to determine the degree of RV dilatation and assessment of RV function.

Tricuspid annular plane systolic excursion (TAPSE) measures the systolic excursion of the RV annular plane toward the apex. It has the advantages of being an easy echocardiographic measurement, can be measured rapidly, and is widely used even if its reliability is controversial(42,43). A TAPSE value of <17 mm is suggestive of RV longitudinal dysfunction in adults. In children, the absolute value of TAPSE must be indexed to the RV longitudinal diameter(TAPSE/RV longitudinal diameter ratio lower than 25% suggests longitudinal dysfunction)(44). Limitations of TAPSE include, in patients with severe RV hypertrophy radial contraction becomes the predominant direction of RV systolic deformation(45) and while measuring the longitudinal deformation, TAPSE may underestimate the real systolic function(8). Secondly, another factor that may reduce the sensitivity of TAPSE in the assessment of systolic function is the fact that TAPSE is strongly preload dependent.

Sustained ventricular tachycardia and sudden cardiac death are known to be associated with increasing RV dimensions. Kavey et al studied 38 post-surgical ToF patients with M mode echocardiography and radionuclide ventriculography to assess whether subclinical levels of ventricular dysfunction in these patients is associated with the development of ventricular arrhythmias. They noted that patients that develop ventricular arrhythmias had a significantly more dilated right ventricle and had ventricular dysfunction as assessed by radionuclide ventriculography(46).

Daliento et al studied 66 post-surgical ToF patients who underwent repair by ventriculotomy to assess the prognostic significance of non-invasive clinical diagnostic indices as predictors of ventricular tachycardia and ventricular fibrillation. The mean age of the study population was 11.8 years and the mean duration of follow-up was 16.1 years. They noted that 28.7% of patients developed ventricular arrhythmias (on ECG

or 24 hour Holter monitoring). Non sustained ventricular tachycardia was noted in 10.6% of patients and sustained VT or VF was present in 9% of patients. The authors noted that an increased right ventricular end-diastolic volume (RVEDV) was the most significant marker for malignant ventricular arrhythmias(47).

The use of continuous-wave Doppler is helpful in the measurement of pulmonary gradient and allows the estimation of the severity of pulmonic stenosis. This is however unreliable in conditions where there is a suboptimal alignment of the ultrasound beam with the pulmonary flow, in the presence of pulmonary hypertension and peripheral pulmonary stenosis. Peripheral pulmonary stenosis and pulmonary hypertension lead to a reduction in the anterograde peak gradient which can, in turn, lead to an underestimation in the severity of stenosis. Also, if the velocity of Tricuspid regurgitation exceeds the velocity of pulmonary flow, the severity of pulmonic stenosis can be underestimated. Branch pulmonary artery stenosis is more common than pulmonary hypertension in ToF patients and should be ruled out at the time of pulmonary valve replacement.



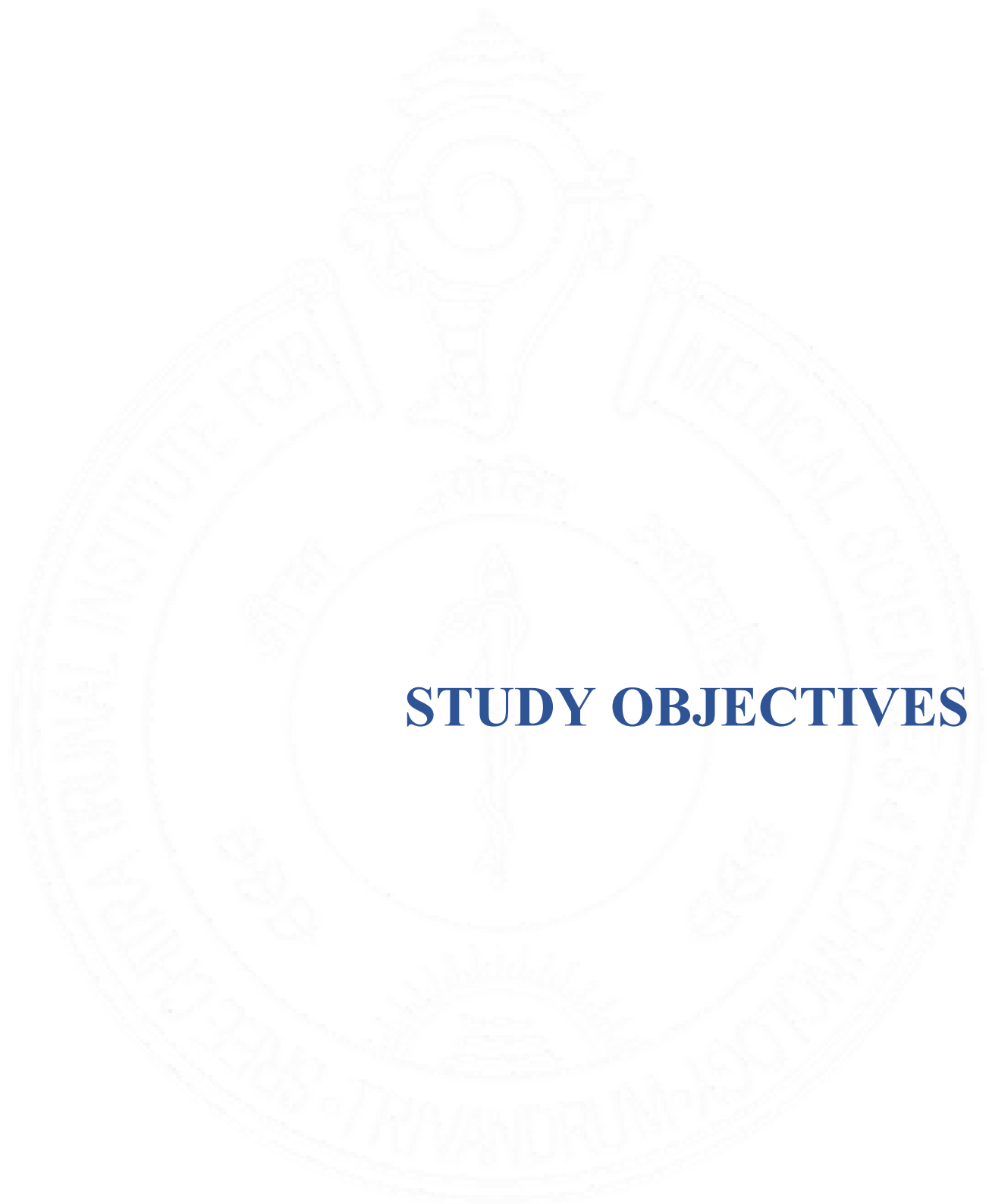
## **AIM AND HYPOTHESIS**

**AIM:**

To describe the arrhythmic complications in post-surgical Tetralogy of Fallot patients.

**HYPOTHESIS:**

Post-surgical Tetralogy of Fallot patients have a high risk of developing arrhythmias secondary to the formation of pro-arrhythmic substrates (scar tissue) and right ventricular dilatation and dysfunction after surgery.



## **STUDY OBJECTIVES**

## **PRIMARY OBJECTIVE**

To describe the arrhythmic complications in post-surgical Tetralogy of Fallot patients who underwent surgery between 1999 and 2005.





# **MATERIALS AND METHODS**

**Design:** Retrospective cohort and cross-sectional study

**Setting:** Tertiary referral center, a university-level hospital (SCTIMST)

**Inclusion Criteria:**

All Tetralogy of Fallot patients who underwent surgical correction between 1999 to 2005 identified by a search of an institutional database and by a search of databases from the Departments of Cardiac Surgery and Cardiology.

**Exclusion Criteria**

- Patients not willing to participate in the study
- Arrhythmias documented within 3 months after surgery were excluded

**Sample size-** Based on previous studies that have reported prevalence of arrhythmia ranging from 10%-34%. Assuming 16 % of post-operative TOF patients develop Arrhythmia. To estimate a 95% CI within +/- 4%, a minimum of **350 patients** are required for the study. Assuming patients lost to follow up since 1999, a sample size of **500 patients** is required.

**Methodology**

This is a descriptive single-center study with retrospective case enrolment and cross-sectional follow-up. Patients who underwent surgical correction for ToF from January 1999 to December 2005 were identified by a search of an institutional database and by a search of databases from the Departments of Cardiac Surgery and Cardiology. Data were collected by the principal investigator. All patients were contacted by address/phone and recruited for the study by the investigating cardiologist. The patients were recruited by the investigators considering the inclusion and exclusion criteria. The investigating cardiologist educated the patient regarding the proposed study. A consent form, written either in English or in the Malayalam language, was signed by the patient and a witness. An attempt was made through the local governing bodies to contact the patients/ family members who did not respond to the calls or to the letters sent to the address mentioned. Patients who have died subsequently would be identified by records

maintained in the Cardiac Surgery Department with the help of the Medical social worker in the department.

Patients data on follow up such as an electrocardiogram (ECG) and 2D echocardiography (2D echo) within 2 years of enrollment were collected from the institutional database and analyzed. All patients on follow up who were contacted by telephone were advised a routine ECG, 2D ECHO and 24-hour Holter. Patients who were unable to visit the SCTIMST OPD were advised to undergo the investigations at a nearby hospital and email the reports to the investigator. Follow-up ECG was analyzed for PR interval, QRS duration, axis, QRS fragmentation, corrected QTc, presence of RBBB, incomplete RBBB, right ventricular hypertrophy and strain. Data collected from 2D echo on follow up included left ventricular dimensions and ejection fraction, right ventricular dimension (PLAX view), right ventricular systolic function (TAPSE), right ventricular outflow tract gradient, severity of pulmonary regurgitation and tricuspid regurgitation and right ventricular systolic pressure. Data from further imaging (Cardiac MRI) and electrophysiological study (EP study), if present, were also collected and analyzed.

Ventricular arrhythmias were defined as:

- Premature Ventricular complexes (Multiple, Couplets) on ECG
- Premature Ventricular complexes >240/day(>10 PVC/hour) on 24 hour Holter(37)
- Documented Non-sustained ventricular tachycardia(<30sec) on ECG or Holter
- Documented ventricular tachycardia on ECG or Holter

Atrial arrhythmias were defined as:

- Documented atrial tachycardia, atrial flutter, atrial fibrillation on ECG or Holter

Bradycardia were defined as:

- Documented AV block on ECG or Holter
- Documented Pause >3 sec on Holter

## **Data Analysis**

The data analysis was performed using the SPSS Statistics software for Windows Version 21 by the investigators with the guidance of Prof Sankara Sarma, Department of Biostatistics, SCTIMST. Descriptive statistics for all variable comparisons were performed using appropriate univariate hypothesis tests. Categorical variables were expressed as with-in group percentages and compared for independent samples using either the Pearson's test or Fisher's exact test. Continuous variables were expressed as either mean standard deviation or median depending on the overall variable distribution. Independent sample, single-factor analysis of variance was used for parametric data comparisons, whereas the Mann Whitney *U* test was used for all nonparametric data comparisons.

Potential risk factors for outcomes were evaluated using a regression model and multiple regression analysis was performed for outcomes with P values less than 0.1. Kaplan Meier analysis was done to analysed the incidence of arrhythmias in relation to time. The data will be stored in the personal computer of the principal investigator for a period of three years, maintaining confidentiality.

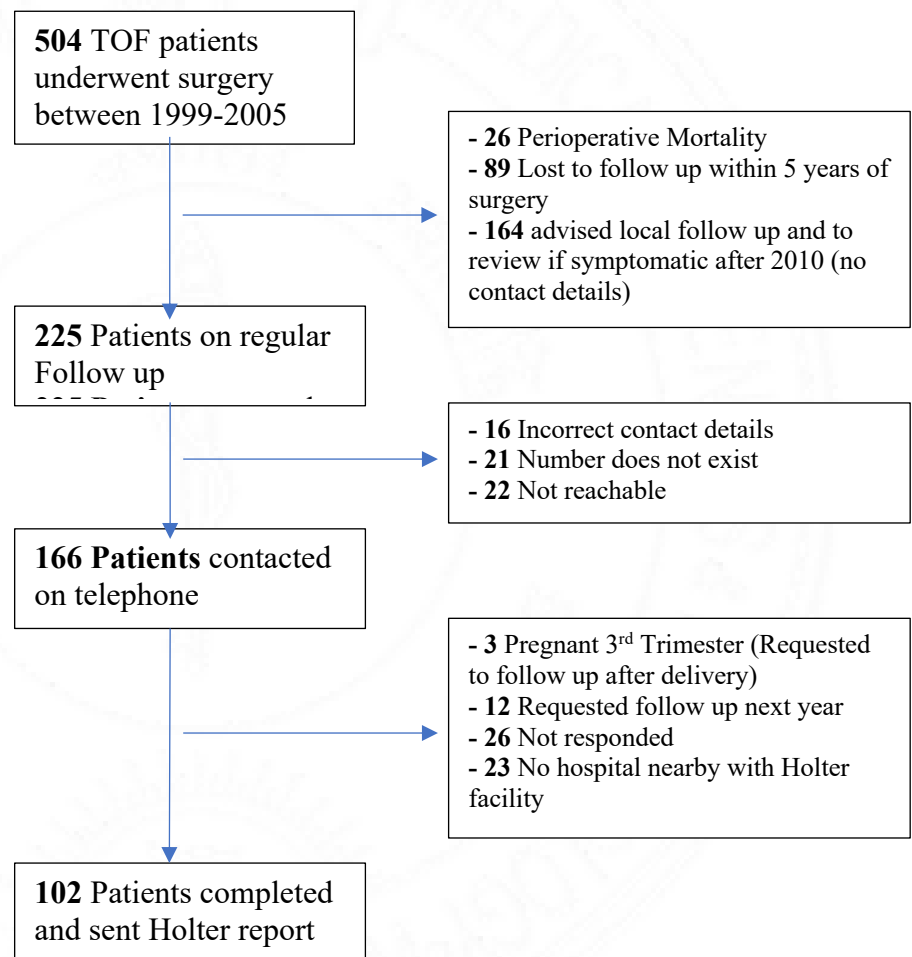


# RESULTS

There were a total of 504 patients who underwent surgical repair for Tetralogy of Fallot (ToF) between 1999-2005. 26 patients had perioperative mortality prior to discharge. 89 patients were lost to follow up within 5 years of the surgery. 166 patients were advised local follow up and to review if symptomatic after 2010 (No contact details were available). 225 patients were on regular follow up and had visited the SCTIMST outpatient department within the last 2 years. 166 patients were contacted on the phone and advised to get a 24 hour Holter report. A total of 102 patients completed the 24 hour Holter.

The following figure depicts the number of patients included(Fig 1)

**Figure 1**



## CHARACTERISTICS OF INCLUDED PATIENTS

**TABLE 1: Baseline clinical characteristics of patients**

Patient Characteristics(n=504)	Observation
Age at Surgery (in yrs) *	<b>5(3-9)</b> [0.5-44]
Gender <sup>‡</sup>	
Males	292(57.9%)
Females	212(42.1%)
Weight (in kg) *	14(10-21)
<b>Pre Op Diagnosis<sup>‡</sup></b>	
TOF	504(100%)
<b>Associated defects<sup>‡</sup></b>	
Branch PA stenosis	46(9.1%)
Absent PV	12(2.3%)
Pulmonary atresia	7(1.3%)
Disconnected PA	1(0.2%)
Coarctation of Aorta	2(0.3%)
Cyanotic Spells <sup>‡</sup>	190(37.7%)
BT shunt <sup>‡</sup>	49(9.7%)
Pre-Op saturation(%) <sup>†</sup>	83.3±5.8
ECHO(pre-op)	
Ejection Fraction(%) [M Mode] *	71(66-76)
<b>LV dimension</b>	
Diastole(mm) *	24(20-29)
Systole(mm) *	15(12-18)
<b>RV dimension(PLAX)(mm) *</b>	15(13-18)
Post Op Saturation(%) <sup>†</sup>	96.4±2.7

TOF- tetralogy of fallot, PA- pulmonary artery, PV- pulmonary valve, BT shunt- Blalock Taussig shunt,

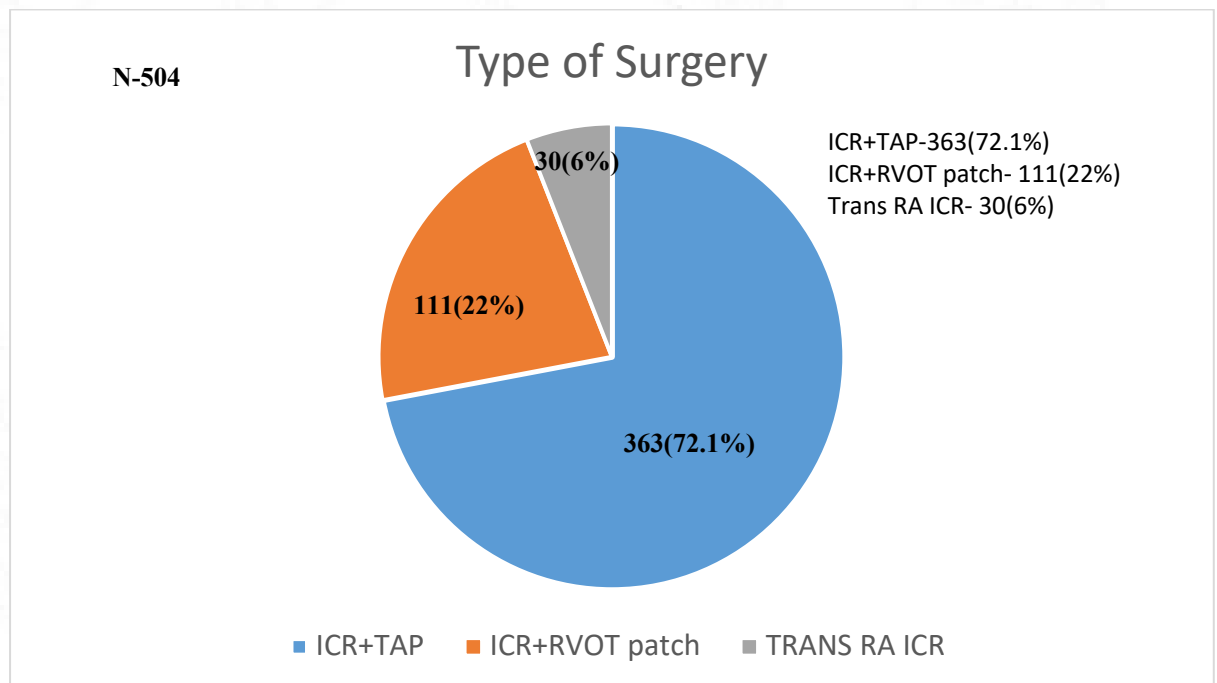
PLAX- parasternal long axis view

\*Median(IQR) † Mean(±SD) ‡ Frequency(%)

The baseline clinical characteristics of the patients are given in Table 1. The median age at the time of surgery was 5(3-9) years. The youngest patient to get operated on was 6 months of age and the oldest was 44 years of age. A majority of them were males 293(57.9%). The median weight at the time of surgery was 14 (10-21) kg. All patients were diagnosed with Tetralogy of Fallot and 68(13.5%) had associated defects, the most common being branch pulmonary artery stenosis 46(9.1%). Cyanotic spells were noted in 190(37.7%) and a BT shunt was a prior surgical procedure in 49(9.7%) patients. The mean pre-op saturation was  $83.3 \pm 5.8$  % and the mean post-op saturation was  $96.4 \pm 2.7$  %.

All patients had a pre-op echocardiogram. The median ejection fraction(M Mode) was 71(66-76) %. The median left ventricular dimensions in diastole was 24(20-29) mm and in systole was 15(12-18) mm. The median RV dimension(PLAX) was 15(13-18) mm

**FIGURE 1: Surgical Technique**



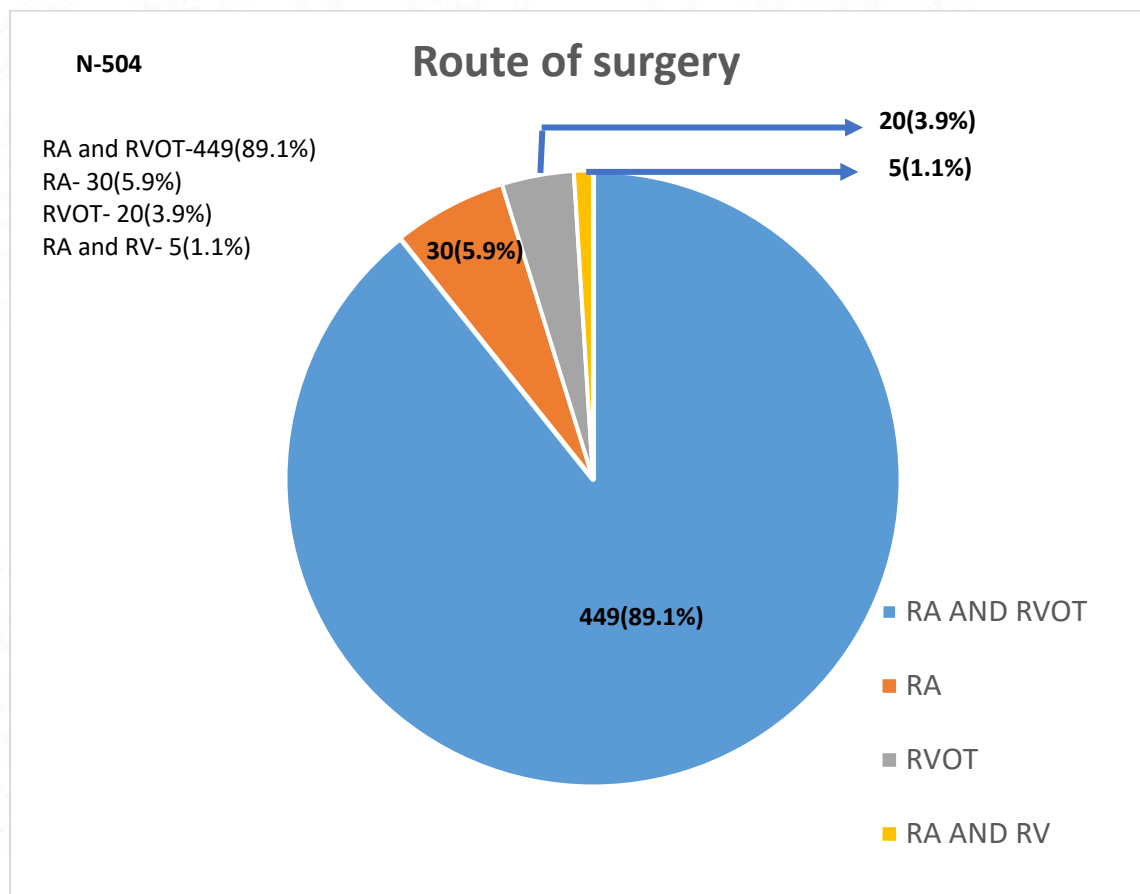
**Additional procedures<sup>‡</sup> - 59(11.7%)**

The surgical techniques used are depicted in Figure 1. The most common surgical technique used was intracardiac repair with a transannular patch (ICR+TAP) in

363(72.1%). This was followed by intracardiac repair with right ventricular outflow tract patch (ICR+RVOT patch) in 111(22%). A trans right atrial intracardiac repair (Trans RA ICR) was done in 30(6%).

The route of surgical repair is depicted in Figure 2. The most common route of repair used was a right atrial incision and right ventricular outflow tract incision (RA and RVOT) in 449(89.1%). This is followed by right atrial incision in 30(5.9%). An RVOT only incision was used in 20(3.9%). A right atrial and right ventricular incision(RA and RV) was used in 5(1.1%) patients.

**FIGURE 2: Route of surgical repair**



The characteristics of the patients on follow up are shown in Table 2. A total of 225(45.04%) were on regular follow-up with a median follow-up duration of 16(15-18) years. A majority comprised of males 128(56.9%). The median age at follow-up was 22(17-26) years. Most patients were asymptomatic (NYHA functional class I)

188(83.6%). A total of 37(16.4%) patients were symptomatic on follow up with the most common symptom being palpitations 21(9.3%). An electrocardiogram (ECG) was available for all patients on follow up. The median PR interval was 160(140-180) ms and the median QRS duration was 130(120-150) ms. Most patients had a normal axis on ECG 177 (78.6%). A complete right bundle branch block was present in 160(71.1%) patients. Right ventricular hypertrophy was present in 80(35.5%) patients and fragmented QRS complexes were noted in 21(9.3%) patients. The median corrected QT was 447(432-465) ms.

**TABLE 2: Characteristics of patients on follow up**

<b>Patient Characteristics</b>	<b>Observation</b>
<b>Patients currently on follow up<sup>†</sup></b>	<b>225(45.04%)</b>
<b>Follow up duration(years) *</b>	<b>16(15-18)</b>
<b>Present Age (in yrs) * (N-225)</b>	<b>22(17-26)</b> [2-59]
<b>Gender<sup>‡</sup> (Follow up) (N-225)</b>	
Male	128(56.9%)
Female	97(43.1%)
<b>NYHA Functional Class (N-225)</b>	
Class I <sup>†</sup>	188(83.6%)
Class II <sup>†</sup>	34(15.1%)
Class III <sup>†</sup>	2(0.8%)
Class IV <sup>†</sup>	1(0.4%)
<b>Symptomatic on follow up<sup>†</sup> (n-225)</b>	37(16.4%)
Palpitations <sup>‡</sup>	21(9.3%)
Dyspnea on exertion <sup>‡</sup>	11(4.8%)
Syncope <sup>‡</sup>	5(2.2%)
<b>ECG(On follow up) (n-225)</b>	
PR(ms) *	160(140-180)
QRSd (ms) *	130(120-150)
Axis – Normal <sup>†</sup>	177(78.6%)
Right Axis Deviation <sup>‡</sup>	41(18.2%)

Left Axis Deviation <sup>†</sup>	7(3.1%)
Axis(Measured)[degrees] *	90(60-105)
RBBB <sup>‡</sup>	160(71.1%)
iRBBB <sup>‡</sup>	45(20.1%)
No RBBB <sup>‡</sup>	20(8.8%)
RBBB with Left Axis Deviation	7(3.1%)
RVH <sup>‡</sup>	80(35.5%)
RV strain <sup>‡</sup>	41(18.2%)
Fragmented QRS <sup>‡</sup>	21(9.3%)
QTc(ms) *	447(432-465)

NYHA- New York heart Association, QRSd-QRS duration, RBBB- right bundle branch block, RVH- right ventricular hypertrophy, QTc- Corrected QT interval

\*Median(IQR) † Mean(±SD) ‡ Frequency(%)

**TABLE 3: Echocardiographic Characteristics of patients on follow up**

Patient Characteristics	Observation
<b>ECHO (On follow up) (N-225)</b>	
EF(%) [M Mode] *	65(61-71)
<b>LV dimension</b>	
Diastole(mm) *	39(35-43)
Systole(mm) *	24(22-28)
<b>RV dimension (PLAX)(mm) *</b>	28(25-33)
TAPSE(mm) *	19(17-20)
RVOT peak(mmHg) *	20(14-27)
RVOT mean(mmHg) *	11(8-15)
RVSP(mmHg) *	30(25-35)
Tricuspid Regurgitation <sup>‡</sup>	
1	78(34.6%)
2	95(42.2%)
3	38(16.8%)

4	14(6.2%)
Pulmonary Regurgitation <sup>†</sup>	
1	24(10.6%)
2	70(31.1%)
3	83(36.8%)
4	48(21.3%)
Residual VSD <sup>‡</sup>	20(8.8%)

EF- ejection fraction, PLAX- parasternal long axis, RVOT- right ventricular outflow tract, TAPSE- tricuspid annular plane systolic excursion, RVSP right ventricular systolic pressure, VSD- ventricular septal defect

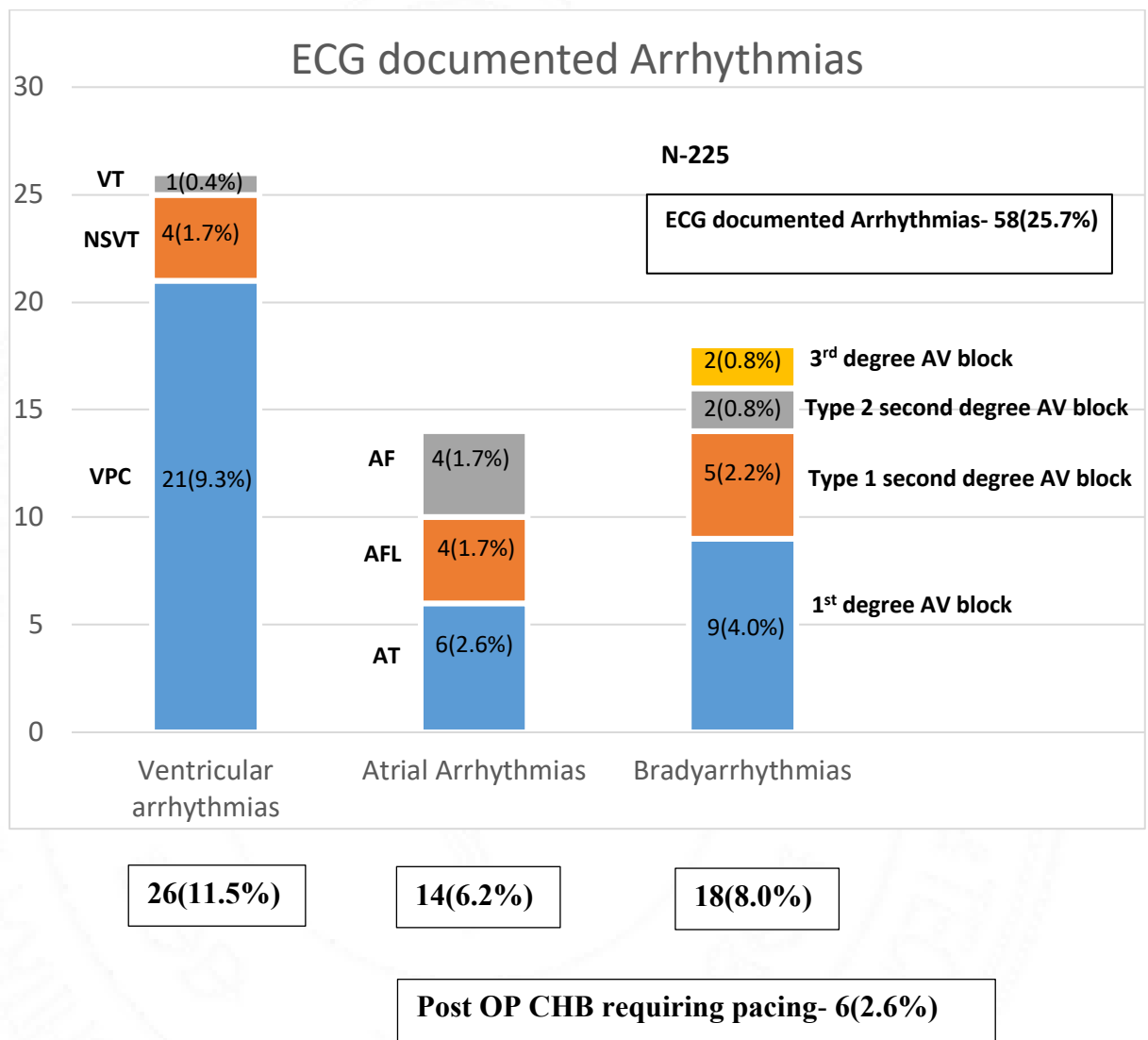
\*Median(IQR) † Mean( $\pm$ SD) ‡ Frequency(%)

All patients had echocardiography done on follow up and details are depicted in Table 3. The median ejection fraction by M mode was 65(61-71) % and median left ventricular diastolic and systolic dimensions were 39(35-43) mm and 24(22-28) mm respectively. The median right ventricular dimension (PLAX) was 28(25-33)mm. The median TAPSE was 19(17-20) mm. Median Right ventricular outflow tract peak and mean gradients were 20(14-27) mmHg and 11(8-15) mmHg. Majority of patients mild or trivial tricuspid regurgitation 173(76.8%). Moderate pulmonary regurgitation was noted in 83(36.8%) patients and severe pulmonary regurgitation was present in 48(21.3%) patients.

Arrhythmias documented on the ECG on follow-up are shown in Figure 3 as a vertical stacked bar chart. A total of 58(25.7%) patients had arrhythmias documented on ECG on follow up. Ventricular arrhythmias were documented in 26(11.5%) patients. These are mainly comprised of ventricular premature complexes (Multiple, Couplets, Trigemini) in 21(9.3%) patients. 4(1.7%) had documented non-sustained ventricular tachycardia (NSVT) on ECG and sustained ventricular tachycardia was documented in 1(0.4%) patient. Atrial arrhythmias were documented in 14(6.2%) patients on follow-up ECG. Atrial tachycardia was noted in 6(2.6%) patients, 4(1.7%) had atrial flutter and atrial fibrillation was noted in 4(1.7%) patients. Bradyarrhythmias were

documented in 18(8%) patients. 9(4%) had first degree AV block, 5(2.2%) patients had type 1 second degree AV block, 2(0.8%) patients had type 2 second degree AV block and third-degree AV block was noted in two patients on follow up (Both patients had a pacemaker implanted).

**FIGURE 3: ECG documented Arrhythmias**



VPC- ventricular premature complex, NSVT- non sustained ventricular tachycardia, VT- ventricular tachycardia, AT- atrial tachycardia, AFL- atrial flutter, AF- atrial fibrillation

A 24-hour Holter was done for 102 patients on follow up. The 24-hour Holter details are shown in Table 4 and the Holter documented arrhythmias are depicted in Figure 4 as a vertical stacked bar chart. The median average heart rate was 68(63-73) beats/min. Ventricular premature complex burden(>10 VPCs/hour) was noted in 14(13.7%) patients. Non sustained ventricular tachycardia runs were noted in 4(3.8%) patients. Arrhythmias were documented in 28(27.4%) patients. Ventricular arrhythmias were noted in 18(17.6%) patients [Ventricular premature complexes >240/day in 14(13.7%) patients and NSVT runs in 4(3.8%) patients]. Atrial arrhythmias were documented in 4(3.9%) patients [ Atrial tachycardia in 1(0.9%) and atrial fibrillation in 3(2.9%) patients]. Bradyarrhythmias were noted in 6(5.8%) patients [1<sup>st</sup> degree AV block in 3(2.9%) patients, Type 1 second degree AV block in 2(1.9%) patients, and type 2 second degree AV block in 1(0.9%) patient

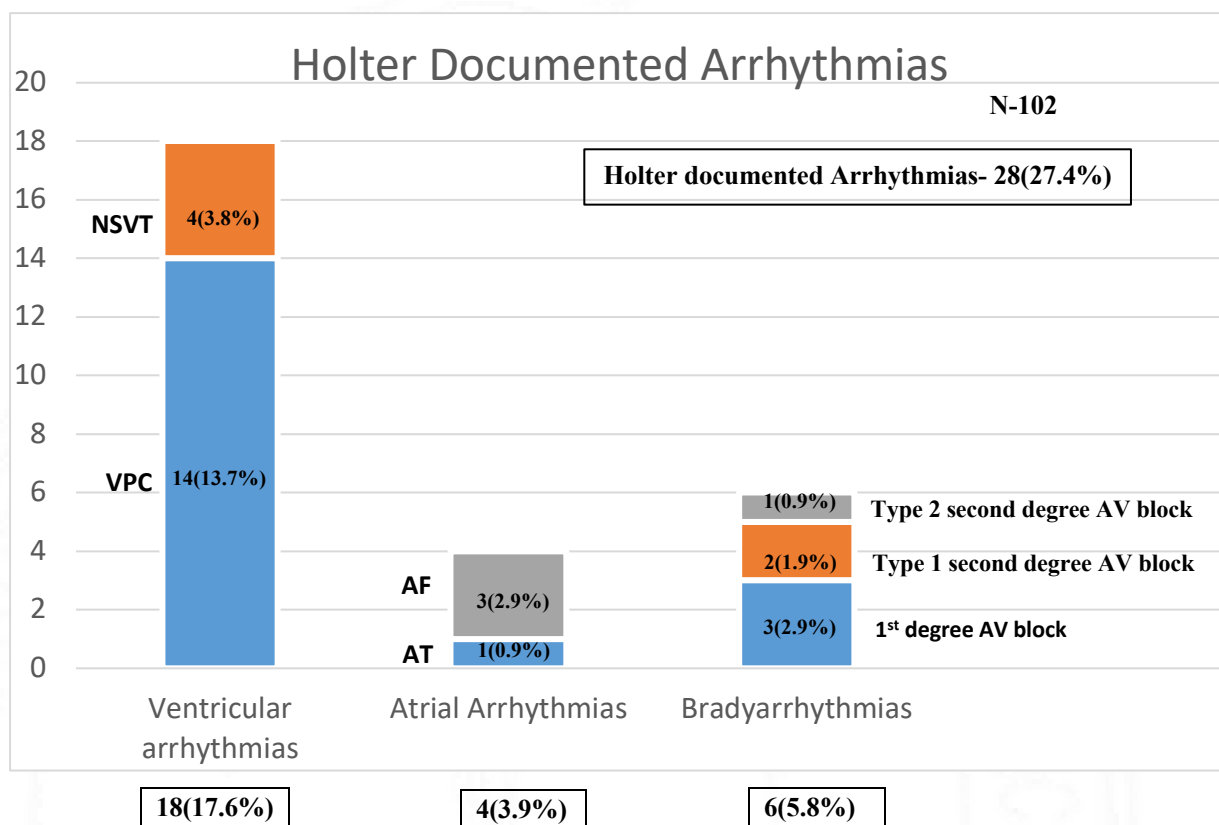
**TABLE 4: Holter Details**

Holter Details	Observation
<b>Holter (On follow up) (N-102)</b>	
Min HR (beats/min) *	48(43-53)
Max HR (beats/min) *	134(125-142)
Avg HR (beats/min) *	68(63-73)
VPC burden (>10 VPCs per hour) †	14(13.7%)
NSVT runs ‡	4(3.8%)
Pause(sec) †	1.8±0.3

HR- heart rate, VPC- ventricular premature complex, NSVT- non sustained ventricular tachycardia

\*Median(IQR) † Mean(±SD) ‡ Frequency(%)

**FIGURE 4: Holter Documented Arrhythmias**



VPC- ventricular premature complex, NSVT- non sustained ventricular tachycardia, VT- ventricular tachycardia, AT- atrial tachycardia, AFL- atrial flutter, AF- atrial fibrillation

**TABLE 5: Medication Details**

<b>Medications</b>	<b>Observation</b>
<b>Medications<sup>†</sup> (N-225)</b>	<b>39(17.3%)</b>
<b>[N-39]</b>	<b>[N-39]</b>
Betablocker <sup>‡</sup>	35(89.7%)
Sotalol <sup>‡</sup>	3(7.6%)
Amiodarone <sup>‡</sup>	4(10.2%)
Anticoagulation <sup>‡</sup>	
- Warfarin	4(10.2%)
- Acitrom	2(5.1%)
Diuretics <sup>‡</sup>	10(25.6%)
ACE Inhibitor <sup>‡</sup>	5(12.8%)
Antiplatelet <sup>‡</sup>	10(25.6%)
Digoxin <sup>‡</sup>	4(10.2%)
Statin <sup>‡</sup>	3(7.6%)
NOAC(Dabigatran) <sup>‡</sup>	2(5.1%)

\*Median (IQR) † Mean( $\pm$ SD) ‡ Frequency(%)

The medication details of patients on follow up are shown in Table 5. Most patients 186(82.6%) were not on any medications on follow up. A total of 39(17.3%) were on medications and the most commonly used medication was beta-blockers.

Cardiac MRI (Cardiac Magnetic Resonance Imaging) was done in all patients who were detected to have severe pulmonary regurgitation (PR) and right ventricular dysfunction/dilatation on 2D echocardiography. The MRI details are shown in Table 6. A total of 24 patients underwent MRI on follow up. The mean right ventricular end-diastolic volume index (RVEDVI) was  $123.8\pm 38.16$  ml/m<sup>2</sup> and the mean right ventricular end-

systolic volume index (RVESVI) was  $70.9 \pm 31.08$ . The mean left ventricular ejection fraction (LVEF) was  $58.4 \pm 8.01$  % and the mean right ventricular ejection fraction (RVEF) was  $45.01 \pm 9.04$  %. The mean pulmonary regurgitant fraction was  $46.2 \pm 13.1$ %. Late Gadolinium Enhancement (LGE) was present in 18 patients (13 at RVOT and 5 at VSD patch). One patient with severe right ventricular dysfunction had a right ventricular apical thrombus detected on MRI.

**TABLE 6: Details of Magnetic Resonance Imaging (MRI)**

<b>MRI Details</b>	<b>Observation</b>
<b>MRI<sup>‡</sup>(N-225)</b>	<b>24(10.4%)</b>
<b>[N-24]</b>	<b>[N-24]</b>
RVEDVI(ml/m <sup>2</sup> ) †	123.8±38.16
RVESVI(ml/m <sup>2</sup> ) †	70.9±31.08
LVEF(%)†	58.4±8.01
RVEF(%)†	45.01±9.04
PR(Regurgitant fraction)(%) †	46.2±13.1
LGE <sup>‡</sup>	18(75%)
- RVOT	13(54.16%)
- VSD patch	5(20.8%)
RV thrombus <sup>‡</sup>	1(4.16%)

RVEDVI- right ventricular end diastolic volume index, RVESVI- right ventricular end systolic volume index, LVEF- left ventricular ejection fraction, RVEF- right ventricular ejection fraction, PR- pulmonary regurgitation, LGE- late gadolinium enhancement,

\*Median (IQR) † Mean(±SD) ‡ Frequency(%)

A total of 5(2.1%) patients on follow-up had an electrophysiological study (EP study). The details of the EP study are shown in Table 7. Two patients underwent successful ablation for atrial flutter. One patient underwent a ventricular tachycardia induction study for evaluation of syncope and multiple VPC on Holter. One patient had a 2:1 AV

block documented on ECG at the age of 12 years, underwent an EP study, and was planned for pacemaker implantation at the age of 16 years in view of normal HV interval.

**TABLE 7: Details of Electrophysiology Study (EP Study)**

EP study †		5(2.1%)
Age(yrs)/Sex	EP study Details	
41/M	1. Atrial flutter- Dual loop reentrant RA flutter - Dominant loop in RA scar and cavotricuspid isthmus- non dominant loop- Successfully Ablated	
22/F	2. History of syncope, multiple VPC on Holter- Patient underwent VT induction – No inducible VT- Implantable Loop recorder (ILR) implanted (2011)- Explanted (2014) –ILR showed Runs of sinus tachycardia- Currently on Medical follow up	
17/M	3. Atrial tachycardia- 2:1 AV RHYTHM, PP INTERVAL 360,? Atrial tachycardia ,?atrial flutter, terminated by atrial overdrive pacing at 260MS- Currently on medical follow up (No recurrence)	
14/F	4. 2:1 AV block- RR interval 1380ms, AA interval 694ms, AH interval 110ms, HV interval -42ms, no preexcitation, occasional AV Wenkebaching with RBBB aberrancy preceded by short cycles- Planned for Pacemaker implantation at 16 years of age.	
59/M	5. Atrial Flutter Cycle length- 250ms, scar related small fragmented potential at the tricuspid annulus, dual AV nodal physiology – Successful Ablation done	

\*Median(IQR) † Mean(±SD) ‡ Frequency(%)

**TABLE 8: Re-operation Details**

Re-operation Details(N-504)	Observation
PVR <sup>‡</sup>	8(1.5%)
Surgical closure of residual VSD <sup>†</sup>	5(0.9%)
Redo ICR+TAP <sup>‡</sup>	3(0.5%)

PVR- Pulmonary Valve Replacement, VSD- ventricular septal defect, ICR+TAP- Intracardiac repair + transannular patch

\*Median(IQR) † Mean( $\pm$ SD) ‡ Frequency(%)

A total of 16(3.1%) patients underwent a re-operation on follow up (Details are shown in Table 8). Pulmonary valve replacement was done for 8(1.5%) patients, residual VSD surgical closure 5(0.9%) patients and redo ICR+TAP was done in 3(0.5%) patients.

**TABLE 9: Mortality Details**

Mortality Details (N-504)	Observation
Perioperative Mortality <sup>‡</sup>	26(5.1%)
Mortality on follow up <sup>‡</sup>	6(1.2%)
- Infective Endocarditis- <1 year	5(1.09%)
- Diagnosed as RHD, severe MS, Severe MR acute pulmonary edema on follow up(2010)- Cardiogenic shock	1(0.2%)

\*Median (IQR) † Mean( $\pm$ SD) ‡ Frequency(%)

Mortality details of patients are depicted in Table 9. Perioperative mortality was noted in 26(5.1%) patients. A total of 6 patients expired on follow up with 5 patients expiring due to infective endocarditis within 1 year of surgery. One patient returned 8 years after surgery with acute pulmonary edema and was diagnosed with rheumatic heart disease, severe mitral stenosis, severe mitral regurgitation, and expired due to cardiogenic shock.

**TABLE 10: Univariate analysis for association between baseline patient characteristics and arrhythmias**

Parameter	Ventricular Arrhythmias (p value)	Atrial Arrhythmias (p value)	Bradyarrhythmias (p value)
Age at Surgery(yrs) *	0.409	<0.001	0.811
Sex <sup>‡</sup>	0.382	0.292	0.957
Weight at surgery(kg) *	0.539	<0.001	0.957
BT shunt <sup>‡</sup>	<b>0.014</b>	0.181	0.152
SpO2(Pre op) †	<b>0.069</b>	0.479	0.799
Surgical Procedure <sup>‡</sup>	0.981	0.633	0.282
Route of Surgical Approach <sup>‡</sup>	0.294	0.595	0.167
SpO2(Post op) †	0.782	0.563	0.432
EF(pre Op) *	0.210	0.374	0.589
LV dimension(Pre Op- Systolic) *	<b>0.085</b>	<b>0.005</b>	0.740
LV dimension(Pre Op- Diastolic) *	0.159	<b>0.008</b>	0.476
RV dimension Pre op [PLAX](mm) *	0.123	<b>0.05</b>	0.730

\* p value calculated using Mann-Whitney U test

† p value calculated using Unpaired t-test

‡ p value calculated using Chi-square test

Univariate analysis was done to assess the association between baseline patient characteristics and arrhythmias. The presence of a prior BT shunt, Low pre-op saturation, and pre-op left ventricular systolic dimension were found to be significantly associated with the presence of ventricular arrhythmias on follow up. The age at surgery, weight at surgery, pre-op left ventricular systolic and diastolic dimensions, and pre-op right ventricular dimension (PLAX) were found to be significantly associated with the presence of atrial arrhythmias on follow up. Bradyarrhythmias were not significantly associated with any baseline parameter.

**TABLE 11: Univariate analysis for association between patient characteristics on follow up and arrhythmias**

Parameter	Ventricular Arrhythmias (p value)	Atrial Arrhythmias (p value)	Bradyarrhythmias (p value)
Present Age (in yrs) *	0.923	0.006	0.857
Follow up Duration*	0.214	0.295	<b>0.018</b>
<b>ECG(on follow up)</b>			
Rhythm <sup>‡</sup>	0.550	<b>&lt;0.001</b>	0.163
PR(ms) *	0.285	0.835	<b>&lt;0.001</b>
QRS duration(ms) *	0.328	0.784	0.252
Presence of RBBB <sup>‡</sup>	0.739	0.295	0.223
Presence of iRBBB <sup>‡</sup>	0.768	0.318	0.801
Axis <sup>‡</sup>	0.494	0.786	0.650
Presence of RBBB+ Left Axis Deviation <sup>‡</sup>	0.730	0.606	<b>0.011</b>
RVH <sup>‡</sup>	0.667	0.381	0.423
RV strain <sup>‡</sup>	0.415	0.669	0.466
Fragmented QRS <sup>‡</sup>	0.566	0.121	0.660
QTc(ms) *	0.889	0.954	0.770
NYHA functional Class <sup>‡</sup>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.930
Symptoms on follow up <sup>‡</sup>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	0.104
<b>ECHO(on follow up)</b>			
EF(%) *	<b>0.086</b>	0.621	0.662
LV dimensions(Systolic mm) *	0.526	<b>0.009</b>	0.398
LV dimension(Diastolic mm) *	0.879	<b>0.023</b>	0.291
RV dimension[PLAX](mm) *	0.540	<b>&lt;0.001</b>	0.326
TAPSE(mm) *	0.691	<b>0.003</b>	0.644
Severity of TR <sup>‡</sup>	0.192	0.160	0.434
Severity of PR <sup>‡</sup>	0.312	0.211	0.692
RVOT peak(mmHg) *	0.648	0.317	0.272
RVSP(mmHg) *	0.662	0.980	0.134
<b>MRI(n-24)</b>			
RVEDVI(ml/m2) †	0.784	0.209	0.651
RVESVI(ml/m2) †	0.648	0.870	0.651
LVEF(%) †	0.966	0.869	0.649
RVEF(%) †	0.958	0.171	0.130
PR(RF)(%) †	0.313	0.207	0.269
LGE <sup>‡</sup>	0.338	0.981	0.115

\* p value calculated using Mann-Whitney U test

† p value calculated using Unpaired t-test

‡ p value calculated using Chi-square test

Univariate analysis of patient characteristics on follow-up showed that NYHA functional class, presence of symptoms, left ventricular ejection fraction were

significantly associated with the presence of ventricular arrhythmias on follow up. The presence of atrial arrhythmias on follow up was significantly associated with the presence of non-sinus rhythm, NYHA functional class, presence of symptoms, left ventricular dimensions in systole and diastole, increased right ventricular dimension [PLAX], and a reduced TAPSE. Follow up duration, PR interval, and presence of RBBB and left axis deviation were significantly associated with the presence of bradyarrhythmias on follow up.

**TABLE 12: Multiple logistic regression of variables found to be significant in univariate analysis for Ventricular arrhythmias**

Parameter	Ventricular Arrhythmias	
	Odds ratio(95% CI)	P value
Previous BT shunt	2.73(0.74-9.99)	0.12
Pre Op SpO2	0.93(0.83-1.05)	0.28
LV dimension(Diastole)(Pre op)	0.97(0.9-1.04)	0.46
<b>NYHA functional class on follow up</b>	<b>8.2(2.9-23.29)</b>	<b>&lt;0.001</b>
<b>Symptomatic on follow up</b>	<b>7.9(2.5-24.6)</b>	<b>&lt;0.001</b>
Ejection fraction on follow up	1.04(0.96-1.12)	0.32

The baseline and follow-up parameters that were found to be significantly associated with ventricular arrhythmias in the univariate analysis were analyzed with multiple logistic regression to see which factors were independently associated with the presence of ventricular arrhythmias follow-up. A higher NYHA functional class on follow up (more symptomatic status) was found to be independently associated with the presence of ventricular arrhythmias on follow up

**TABLE 13: Multiple logistic regression of variables found to be significant in univariate analysis for Atrial arrhythmias**

Parameter	Atrial Arrhythmias	
	Odds Ratio (95% CI)	P value
Present Age(yrs)	1.08(0.87-1.34)	0.47
Age at surgery(yrs)	1.03(0.76-1.39)	0.83
Weight at surgery(kg)	0.93(0.81-1.06)	0.24
RV dimension(pre op)	1.07(0.80-1.42)	0.64
LV dimension-Systolic(Pre Op)	0.89(0.65-1.21)	0.45
LV dimension-Diastolic(Pre Op)	0.93(0.78-1.10)	0.42
RV dimension (Pre Op)	1.03(0.74-1.44)	0.83
NYHA functional class on follow up	9.25(5.8-24.05)	<b>&lt;0.001</b>
Symptomatic on Follow up	7.2(2.35-21.3)	<b>0.012</b>
TAPSE(mm) on follow up	0.52(0.35-0.77)	<b>0.001</b>
RV dimension[PLAX](on Follow up)	1.4(1.15-1.70)	<b>0.001</b>

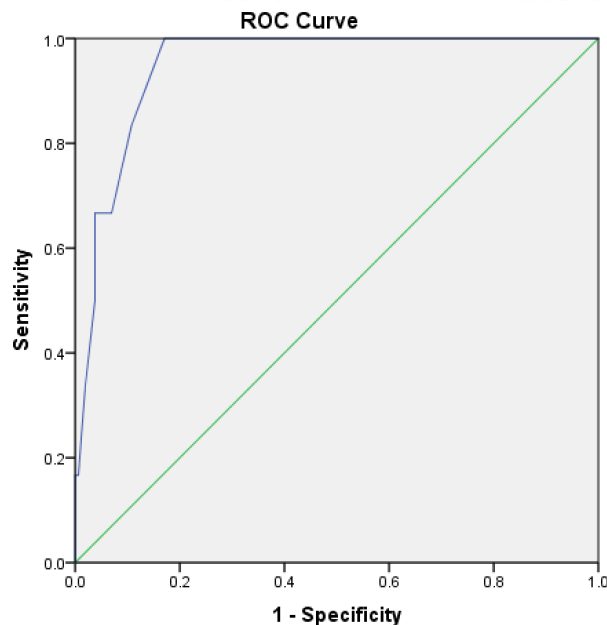
The baseline and follow-up parameters that were found to be significantly associated with atrial arrhythmias in the univariate analysis were analyzed with multiple logistic regression to see which factors were independently associated with the presence of atrial arrhythmias on follow up. A higher NYHA functional class (more symptomatic status), a lower TAPSE (indicating right ventricular dysfunction), and increased right ventricular dimension (PLAX) were found to be independently associated with the presence of atrial arrhythmias on follow-up.

**TABLE 14: Multiple logistic regression of variables found to be significant in univariate analysis for Bradyarrhythmias**

Parameter	Bradyarrhythmias	
	Odds Ratio (95% CI)	P value
Presence of RBBB+Left axis Deviation	7.32(1.23-23.48)	<b>0.029</b>
PR interval(ms)	1.04(1.02-1.31)	<b>0.001</b>
Follow up Duration(yrs)	1.39(1.1-1.95)	<b>0.05</b>

The baseline and follow-up parameters that were found to be significantly associated with bradyarrhythmias in the univariate analysis were analyzed with multiple logistic regression to see which factors were independently associated with the presence of bradyarrhythmias on follow up. The presence of RBBB with left axis deviation, an increased PR interval, and increased follow-up duration were found to be independently associated with bradyarrhythmias on follow up.

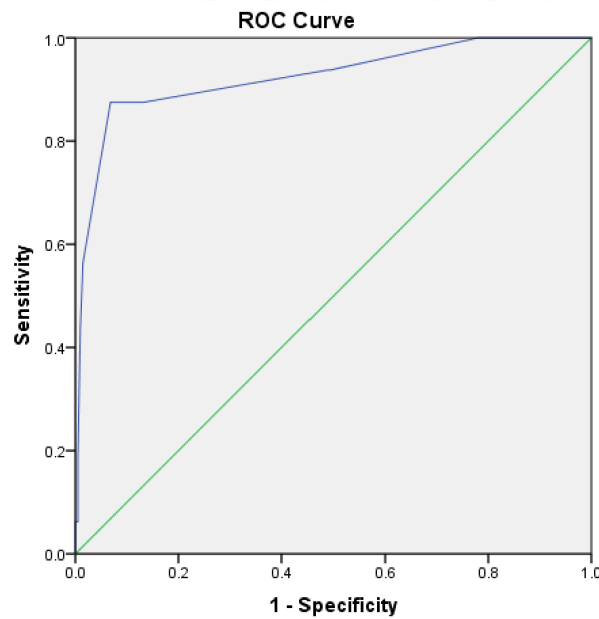
**FIGURE 5: ROC curve for estimation of RV dimension (PLAX) cut off for predicting atrial arrhythmias**



Parameter	AUC	Value(mm)	Sensitivity	Specificity
RV dimension on followup(mm)	0.949	33.5	1.00	0.83

ROC analysis was done to determine the value of the right ventricular(RV) dimension(PLAX) that predicts the occurrence of atrial arrhythmias. A RV dimension(PLAX) greater than 33.5mm predicts the occurrence of atrial arrhythmias with a sensitivity of 100% and specificity of 83% (AUC=0.949).

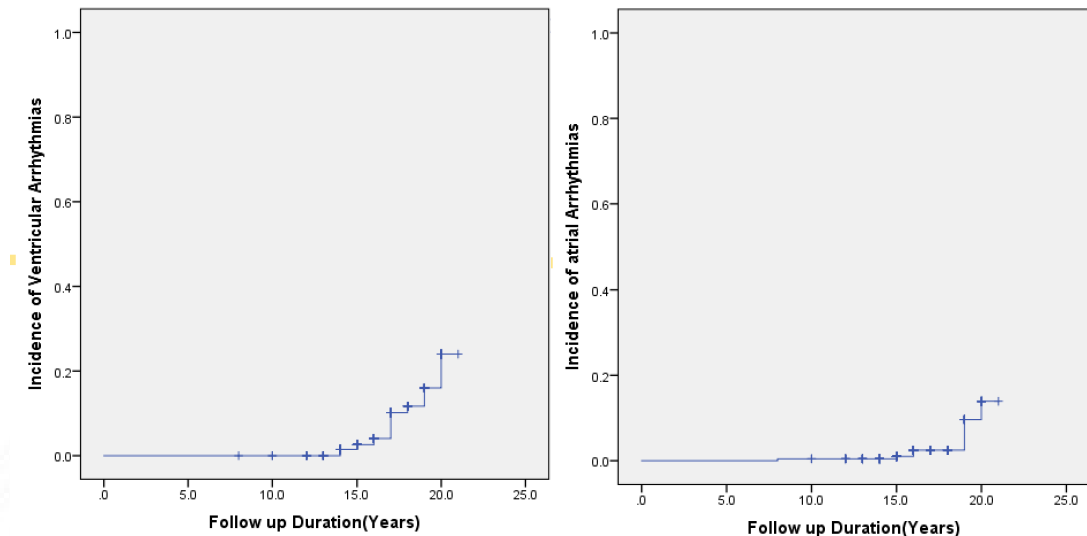
**FIGURE 6: ROC curve for estimation of PR interval cut off for predicting bradyarrhythmias**



Parameter	AUC	Value(ms)	Sensitivity	Specificity
PR interval on Follow up(ms)	0.924	190	0.87	0.88

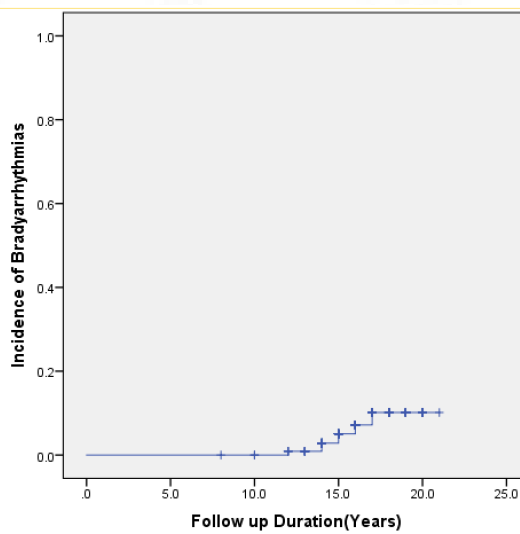
ROC analysis was done to determine the value of PR interval that predicts the occurrence of bradyarrhythmias. A PR interval greater than 190ms predicts the occurrence of bradyarrhythmias with a sensitivity of 87% and specificity of 88% (AUC=0.924).

**FIGURE 7: Kaplan Meier curves showing the incidence of ventricular arrhythmias(a), atrial arrhythmias(b) and bradyarrhythmias(c) with respect to follow up duration(years)**



(a)

(b)



(c)

Kaplan Meier Curve analysis for the incidence of ventricular, atrial and bradyarrhythmias in relation to time are shown in Figure 7.



# **DISCUSSION**

This study was done to assess the arrhythmic complications in patients who had undergone surgical repair for Tetralogy of Fallot (ToF) between 1999-2005. Most patients (83.6%) were asymptomatic (NYHA Functional Class I) on follow up. Arrhythmias were detected in 25.7% of patients on a routine electrocardiogram and in 27.4% of patients on a 24-hour Holter study on follow up. Patients with ventricular arrhythmias were more symptomatic on follow up. A higher right ventricular dimension (PLAX) and right ventricular dysfunction (lower TAPSE) on follow-up were independently associated with the development of atrial arrhythmias. Bradyarrhythmias on follow-up were independently associated with the presence of right bundle branch block (RBBB) with left axis deviation (LAD)[RBBB+LAD], increased PR interval, and increased duration of follow up.

The median age on follow-up of patients included in this study was 22(17-26) years, the median duration of follow-up was 16(15-18) years. This is similar to a multicenter study by Nakazawa et al which showed a mean age on follow-up to be 23.4±9.3 years and mean duration on follow-up was 11.7±7.2 years(21). The majority of patients in our study comprised of males (56.9%). This is in contrast to a study by Khairy et al which noted 54% of the study population to be female(20). Most patients (83.6%) were asymptomatic ( NYHA functional class I) on follow up. This is similar to a study by Garson et al, which analyzed the late outcomes and causes of late death in post-operative ToF patients and noted that 81% of patients were in NYHA functional class I(23). Another study by Gatzoulis et al with a mean duration of follow-up of 21.1 years also noted that 81.8% of patients were NYHA functional class 1.

The surgical technique used most commonly in our study was intracardiac repair with a transannular patch (ICR+TAP) and was used in 72.1% of patients. This is similar to the study by Khairy et al where a transannular patch was also the most commonly used surgical technique in 80.4% of patients.

The median QRS duration on routine follow up electrocardiogram in our study was 130(120-150) milliseconds. In the study by Khairy et al, the mean QRS duration was 150±28 milliseconds. Studies have shown that QRS duration in post-operative ToF patients increases with a longer duration of follow up and the rate of increase identifies

patients at risk of developing ventricular arrhythmias(27). This also explains the higher QRS duration in the study by Khairy et al as the duration of follow-up was significantly higher than our study.

Complete right bundle branch block (Complete RBBB) was the most common conduction disturbance noted in our study in 71.1% of patients, incomplete RBBB was present in 20.1% and RBBB with left axis deviation was noted in 3.1% of patients. This is similar to data from previous studies which documented the prevalence of right bundle branch block to ranging from 59% to 100% (48). In a study by Garson et al which analyzed the late complications after surgical repair of ToF, complete RBBB was noted in 88% of patients and RBBB with left axis deviation was noted in 9.2% of patients.

In our study, moderate and severe pulmonary regurgitation was noted in 36.8% and 29.3% of patients respectively. Moderate or severe tricuspid regurgitation was noted in 16.8% and 6.2% of patients respectively. These findings are similar to the study by Khairy et al where moderate or severe pulmonary regurgitation and tricuspid regurgitation were noted in 47.6% and 15.3% of patients respectively.

Cardiac magnetic resonance imaging (CMRI) was done in 10.6% of patients. The mean right ventricular end diastolic volume index (RVEDI) was  $123.8 \pm 38.16$  ml/m<sup>2</sup> and the mean right ventricular end systolic volume index (RVESVI) was  $70.9 \pm 31.08$  ml/m<sup>2</sup>. A study by Niezen et al who compared CMRI findings of post-surgical ToF patients with normal control subjects. They performed cardiac MRI in 18 post-operative ToF patients with a follow up of 10 years and noted that the mean RVEDVI was  $119 \pm 36$  ml/m<sup>2</sup> and mean RV end systolic volume index was  $57 \pm 30$  ml/m<sup>2</sup>. The right ventricular volumes are higher in our study likely due to the longer duration for follow up ( median 16 years vs mean 10 years). The mean right ventricular ejection fraction (RVEF) in our study was  $45.01 \pm 9.04\%$  and mean left ventricular ejection fraction (LVEF)  $58.4 \pm 8.01\%$ . The Niezen et al study noted that the RVEF was  $54 \pm 8\%$  and LVEF was  $52 \pm 10\%$ (49). The lower RVEF in our study is again likely due to the longer duration of follow up and increased right ventricular volumes on follow up. The mean pulmonary regurgitation fraction in our study was  $46.2 \pm 13.1\%$ . This is similar to the study by Vleigen et al which analysed CMRI findings to assess the hemodynamic

effects of pulmonary valve replacement (PVR) after repair of ToF. In that study, the mean pulmonary regurgitation fraction was  $46 \pm 10\%$  (with median duration between initial repair and PVR of 24.2 years)(50).

Arrhythmias were documented in routine electrocardiogram(ECG) in 25.7% of patients and on 27.4% of patients on 24 hour Holter study. The prevalence of arrhythmias documented in our study is higher than the study by Nakazawa et al (10.5% with a mean follow up duration of 11.7 years) and lower than the study by Khairy et al (29.9% with a mean follow up duration of 35 years)(20,21). These results are also similar to other studies which noted that patients were relatively asymptomatic until 10-15 years after surgery followed by a steady increase in atrial and ventricular arrhythmias(27,36).

Ventricular arrhythmias were noted in 11.5% of patients on routine ECG and 17.6% of patients on 24 hour Holter study. Ventricular premature complexes were noted in 9.3% of patients, non-sustained ventricular tachycardia(NSVT) in 1.7% of patients, and sustained VT was documented in 1 patient on follow-up ECG. Nakazawa et al noted ventricular arrhythmias in 3.5% of patients and Khairy et al noted ventricular arrhythmias in 14.6% of patients with 14.2 % having sustained ventricular tachycardia. Gatzoulis et al noted ventricular arrhythmias in 3.9% of patients (ventricular tachycardia). The higher number of ventricular arrhythmias in the Khairy et al study can be attributed to the longer duration of follow-up (20,21,27).

Holter documented ventricular arrhythmias were noted in 17.6% of patients in this study( ventricular premature complexes(13.7%), NSVT in 4(3.8%)). Gatzoulis et al also analyzed 24 hour Holter in post-operative ToF patients and noted ventricular arrhythmias in 3.2% of patients and NSVT was noted in 1 patient(27). The higher number of ventricular arrhythmias documented in our study is likely due to the VPC per hour cut off, >10 per hour used in our study during Holter analysis. This cut-off was based on a previous study by Garson et al which analyzed the outcomes of post-surgical ToF patients with specific reference to the treatment of ventricular arrhythmias(37). Kaplan Meier curve analyzing the incidence of ventricular arrhythmias over time shows that the incidence of ventricular arrhythmias gradually increase from approximately 13 years post-surgery. This is similar to the study by Nakazawa et al which showed that ventricular arrhythmias begin to increase around 10 years post-surgery(21)

Atrial arrhythmias were noted in 6.2% of patients in this study (atrial tachycardia (2.6%), atrial flutter (1.7%), atrial fibrillation (1.7%)). This is similar to the study by Nakazawa et al where 3.9% of patients had atrial arrhythmias (atrial tachycardia (0.9%), atrial flutter (1.5%), atrial fibrillation (1.5%)) (21). However, in the study by Khairy et al, the prevalence of atrial arrhythmias was 20% (atrial flutter (11.5%), atrial fibrillation (7.4%)) (20). The study by Khairy et al had a longer follow-up duration which can explain the higher prevalence of atrial arrhythmias. Holter documented atrial arrhythmias in our study were noted to be present in 3.9% of patients. This is similar to the study by Gatzoulis et al which noted atrial flutter/fibrillation in 3.1% of patients on routine ECG on follow up and in 6.3% of patients on a 24 hour Holter (27).

Kaplan Meier curve analysis in our study shows that the incidence of atrial arrhythmias increases with a longer duration follow-up. This is similar to the study by Harrison et al which analyzed the atrial arrhythmias after ToF surgical repair and noted a prevalence of atrial tachycardia of 12% and also showed that the incidence of atrial tachycardia and event rate (cardiac failure, reoperation, ventricular tachycardia stroke, and death), when compared with an arrhythmia free population increased with longer duration of follow up (36).

Right ventricular dilatation (by 2D PLAX) and dysfunction (by TAPSE) were noted to be independently associated with the incidence of atrial arrhythmias. This is similar to the study by Harrison et al which showed increased right ventricular end-diastolic dimension (4 chamber view) was more likely to be present in patients with atrial arrhythmias than in the age-matched comparison group, although the difference was not statistically significant ( $51 \pm 9$  vs  $45 \pm 7$ ,  $p=0.08$ ). The same study also noted that right ventricular systolic dysfunction was more likely to be present in patients with atrial arrhythmias than in the age-matched comparison group but this association was not statistically significant (66% vs 53%,  $p=0.28$ ). The ventricular arrhythmias after ToF surgical repair increases with a longer duration of follow up due to progressive myocardial fibrosis (5). This is also noted with atrial arrhythmias. The substrate for atrial tachycardias is caused by previous surgical incisions at the atriotomy site which undergo fibrosis and result in re-entry around the incisional site (51).

In this study, bradyarrhythmias were noted in 8% of patients (1<sup>st</sup> degree AV block in 4.0%, Type I second degree AV block in 2.2%, Type II second degree AV block in 0.8%, 3<sup>rd</sup> degree AV block in 0.8%). This is similar to the findings by Nakazawa et al where the prevalence of bradyarrhythmias was 4.4%. Another study with similar findings was conducted by Nollert et al analyzed the long term survival in patients after TOF repair with a mean duration of follow up of 25.3 years and noted that the prevalence of bradyarrhythmias was 6.7% (1<sup>st</sup> degree AV block in 5.3%, second degree AV block in 0.8%, 3<sup>rd</sup> degree AV block in 0.6%) (4). Kaplan Meier curve analyzing the incidence of bradyarrhythmias in relation to the duration of follow up shows that the incidence of bradyarrhythmias increases with a longer duration of follow up which is consistent with other studies (4,21).

The presence of right bundle branch block (RBBB) with left axis deviation (LAD) was found to be independently associated with the presence of bradyarrhythmias on follow up. The presence of RBBB with left axis deviation indicates the involvement of the left anterior fascicle (left anterior hemiblock (LAH)). The incidence of RBBB+LAD in our study was 3.1%. Injury to the right bundle and the left anterior fascicle occurs at the time of surgery (52). Wolff et al analyzed the prognostic value of the presence of RBBB with LAH in post-operative ToF and noted that this pattern is associated with an increased incidence of late complete heart block and sudden death (53). Injury to the HIS bundle can also result in RBBB+LAH (54). Kusevska-Maneva et al analyzed the arrhythmias and conduction abnormalities after surgical repair of ToF and noted that the prevalence of RBBB with LAH was 8.69% (48). Jonsson et al studied the electrocardiographic findings associated with survival in post-operative ToF patients and noted that 8.7% of patients had RBBB with LAH (55). Both of these studies included patients who underwent surgery before 1999. The subsequent improvement in surgical techniques may be responsible for the lesser incidence of RBBB with LAH in our study.



# LIMITATIONS

1. This study involved a retrospective analysis of the case records to study the baseline characteristics of patients. The collection of data depended upon the accurate documentation of the anatomical diagnosis, preoperative and postoperative evaluation, the surgical details, and follow up details.
2. It is a single-center study, and the conclusions drawn from our study cannot be generalized to a larger population.
3. There was attrition in the study population to the tune of 54.9% over a median follow up of 16 years. Though every effort was made to contact the patient or their relatives, it is possible that patients lost to follow-up may have died. Patients from neighbouring states were difficult to be contacted either through phone or letters.
4. The unexpected effect of the COVID pandemic hindered regular OPD visits and 24-hour Holter analysis.



# CONCLUSIONS

- ▶ In Post-Surgical Tetralogy of Fallot patients, arrhythmias were documented on follow up 1/4<sup>th</sup> of patients either on ECG or 24-hour Holter.
- ▶ On follow up most patients were clinically in New York Heart Association functional class I (NYHA FC I).
- ▶ Patients with ventricular arrhythmias were more symptomatic on follow up and the incidence of ventricular arrhythmias increased with a longer duration of follow up.
- ▶ Patients with atrial arrhythmias were significantly more symptomatic on follow-up and were independently associated with a dilated right ventricle and with right ventricular dysfunction. Incidence of atrial arrhythmias increased with a longer duration of follow up. Increased right ventricular diastolic dimension (PLAX)(>33.5mm) on follow up is predictive of atrial arrhythmias (100% sensitivity and 83% specificity).
- ▶ Bradyarrhythmias on follow up were independently associated with the presence of right bundle branch block with left axis deviation (RBBB+LAD) and increased PR interval. Incidence of bradyarrhythmias increased with longer duration of follow up. Increased PR interval on follow up electrocardiogram (>190 ms) is predictive of bradyarrhythmias (sensitivity 87% and specificity of 88%).



# **BIBLIOGRAPHY**

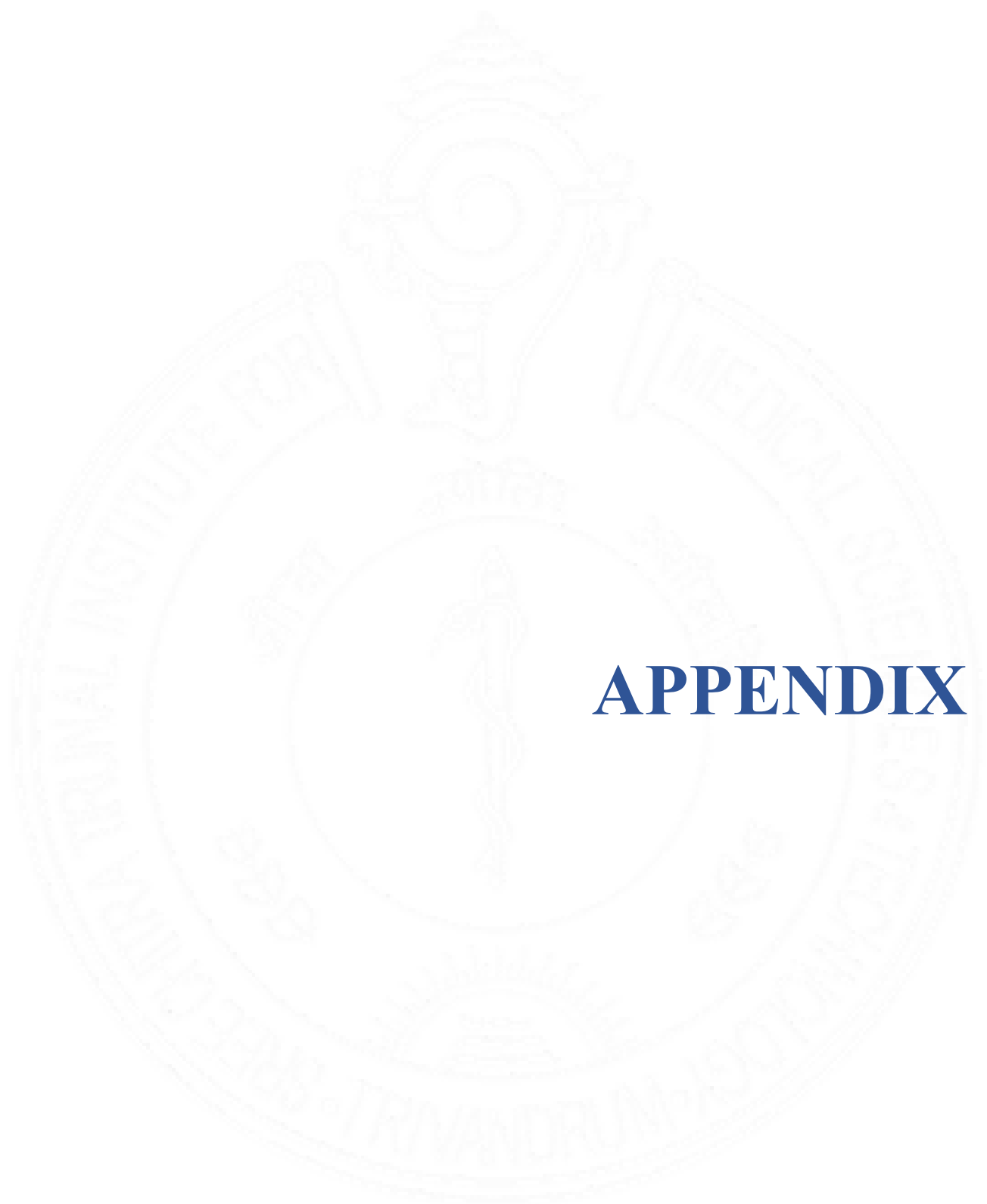
1. Van der Linde D, Konings EEM, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJM, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2011 Nov 15;58(21):2241–7.
2. Lillehei CW, Cohen M, Warden HE, Read RC, Aust JB, DeWall RA, et al. Direct Vision Intracardiac Surgical Correction of the Tetralogy of Fallot, Pentalogy of Fallot, and Pulmonary Atresia Defects. *Ann Surg*. 1955 Sep;142(3):418–42.
3. Nørgaard MA, Lauridsen P, Helvind M, Pettersson G. Twenty-to-thirty-seven-year follow-up after repair for Tetralogy of Fallot. *Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg*. 1999 Aug;16(2):125–30.
4. Nollert G, Fischlein T, Bouterwek S, Böhmer C, Klinner W, Reichart B. Long-term survival in patients with repair of tetralogy of Fallot: 36-year follow-up of 490 survivors of the first year after surgical repair. *J Am Coll Cardiol*. 1997 Nov 1;30(5):1374–83.
5. Deanfield J, McKenna W, Rowland E. Local abnormalities of right ventricular depolarization after repair of tetralogy of Fallot: a basis for ventricular arrhythmia. *Am J Cardiol*. 1985 Feb 15;55(5):522–5.
6. Arthur EL. Dictionnaire des maladies éponymiques et des observations principes : Fallot (tétralogie de). :18.
7. Becker AE, Connor M, Anderson RH. Tetralogy of Fallot: a morphometric and geometric study. *Am J Cardiol*. 1975 Mar;35(3):402–12.
8. Carminati M, Pluchinotta FR, Piazza L, Micheletti A, Negura D, Chessa M, et al. Echocardiographic Assessment after Surgical Repair of Tetralogy of Fallot. *Front Pediatr [Internet]*. 2015 Feb 2 [cited 2020 Nov 13];3. Available from: <http://journal.frontiersin.org/Article/10.3389/fped.2015.00003/abstract>
9. Deanfield JE, McKenna WJ, Presbitero P, England D, Graham GR, Hallidie-Smith K. Ventricular arrhythmia in unrepaired and repaired tetralogy of Fallot. Relation to age, timing of repair, and haemodynamic status. *Heart*. 1984 Jul 1;52(1):77–81.
10. Silka MJ, Hardy BG, Menashe VD, Morris CD. A population-based prospective evaluation of risk of sudden cardiac death after operation for common congenital heart defects. *J Am Coll Cardiol*. 1998 Jul;32(1):245–51.
11. James FW, Kaplan S, Chou TC. Unexpected cardiac arrest in patients after surgical correction of tetralogy of Fallot. *Circulation*. 1975 Oct;52(4):691–5.
12. Misaki T, Tsubota M, Watanabe G, Watanabe Y, Matumoto Y, Ishida K, et al. Surgical treatment of ventricular tachycardia after surgical repair of tetralogy of Fallot. Relation between intraoperative mapping and histological findings. *Circulation*. 1994 Jul;90(1):264–71.
13. Stevenson WG, Delacretaz E, Friedman PL, Ellison KE. Identification and ablation of macroreentrant ventricular tachycardia with the CARTO

- electroanatomical mapping system. *Pacing Clin Electrophysiol PACE*. 1998 Jul;21(7):1448–56.
14. Gatzoulis MA, Till JA, Somerville J, Redington AN. Mechanoelectrical interaction in tetralogy of Fallot. QRS prolongation relates to right ventricular size and predicts malignant ventricular arrhythmias and sudden death. *Circulation*. 1995 Jul 15;92(2):231–7.
  15. Zeppenfeld K, Schalij MJ, Bartelings MM, Tedrow UB, Koplan BA, Soejima K, et al. Catheter ablation of ventricular tachycardia after repair of congenital heart disease: electroanatomic identification of the critical right ventricular isthmus. *Circulation*. 2007 Nov 13;116(20):2241–52.
  16. Zeltser I, Gaynor JW, Petko M, Myung RJ, Birbach M, Waibel R, et al. The roles of chronic pressure and volume overload states in induction of arrhythmias: an animal model of physiologic sequelae after repair of tetralogy of Fallot. *J Thorac Cardiovasc Surg*. 2005 Dec;130(6):1542–8.
  17. Ramos R, Branco L, Agapito A, Oliveira JA, Sousa L, Galrinho A, et al. Usefulness of tissue Doppler imaging to predict arrhythmic events in adults with repaired tetralogy of Fallot. *Rev Port Cardiol Orgao Of Soc Port Cardiol Port J Cardiol Off J Port Soc Cardiol*. 2010 Aug;29(7–8):1145–61.
  18. Mah DY, Alexander ME, Cecchin F, Walsh EP, Triedman JK. The electroanatomic mechanisms of atrial tachycardia in patients with tetralogy of Fallot and double outlet right ventricle. *J Cardiovasc Electrophysiol*. 2011 Sep;22(9):1013–7.
  19. Zubairi R. Arrhythmia Susceptibility and Management in Adult Patients with Repaired Tetralogy of Fallot. *J Clin Exp Cardiol* [Internet]. 2011 [cited 2020 Nov 13];01(02). Available from: <https://www.omicsonline.org/arrhythmia-susceptibility-and-management-in-adult-patients-with-repaired-tetralogy-of-fallot-2155-9880.S3-001.php?aid=2566>
  20. Khairy P, Aboulhosn J, Gurvitz MZ, Opatowsky AR, Mongeon F-P, Kay J, et al. Arrhythmia Burden in Adults With Surgically Repaired Tetralogy of Fallot: A Multi-Institutional Study. *Circulation*. 2010 Aug 31;122(9):868–75.
  21. Nakazawa M, Shinohara T, Sasaki A, Echigo S, Kado H, Niwa K, et al. Arrhythmias Late After Repair of Tetralogy of Fallot. *Circ J*. 2004;68(2):126–30.
  22. Dietl CA, Cazzaniga ME, Dubner SJ, Pérez-Baliño NA, Torres AR, Favaloro RG. Life-threatening arrhythmias and RV dysfunction after surgical repair of tetralogy of Fallot. Comparison between transventricular and transatrial approaches. *Circulation*. 1994 Nov;90(5 Pt 2):II7-12.
  23. Garson A, Nihill MR, McNamara DG, Cooley DA. Status of the adult and adolescent after repair of tetralogy of Fallot. *Circulation*. 1979 Jun;59(6):1232–40.

24. Chandar JS, Wolff GS, Garson A, Bell TJ, Beder SD, Bink-Boelkens M, et al. Ventricular arrhythmias in postoperative tetralogy of Fallot. *Am J Cardiol.* 1990 Mar 1;65(9):655–61.
25. Horowitz LN, Simson MB, Spear JF, Josephson ME, Moore EN, Alexander JA, et al. The mechanism of apparent right bundle branch block after transatrial repair of tetralogy of Fallot. *Circulation.* 1979 Jun;59(6):1241–52.
26. Hazan E, Bical O, Bex JP, Dubuis C, Lecompte Y, De Riberolles C, et al. Is right bundle branch block avoidable in surgical correction of tetralogy of Fallot? *Circulation.* 1980 Oct;62(4):852–4.
27. Gatzoulis MA, Balaji S, Webber SA, Siu SC, Hokanson JS, Poile C, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. *Lancet Lond Engl.* 2000 Sep 16;356(9234):975–81.
28. Balaji S, Lau YR, Case CL, Gillette PC. QRS prolongation is associated with inducible ventricular tachycardia after repair of tetralogy of Fallot. *Am J Cardiol.* 1997 Jul 15;80(2):160–3.
29. Helbing WA, Roest A a. W, Niezen RA, Vliegen HW, Hazekamp MG, Ottenkamp J, et al. ECG predictors of ventricular arrhythmias and biventricular size and wall mass in tetralogy of Fallot with pulmonary regurgitation. *Heart Br Card Soc.* 2002 Nov;88(5):515–9.
30. Shanmugam N, Yap J, Tan RS, Le TT, Gao F, Chan JX, et al. Fragmented QRS complexes predict right ventricular dysfunction and outflow tract aneurysms in patients with repaired tetralogy of Fallot. *Int J Cardiol.* 2013 Aug 20;167(4):1366–72.
31. Park S-J, On YK, Kim JS, Park SW, Yang J-H, Jun T-G, et al. Relation of fragmented QRS complex to right ventricular fibrosis detected by late gadolinium enhancement cardiac magnetic resonance in adults with repaired tetralogy of fallot. *Am J Cardiol.* 2012 Jan 1;109(1):110–5.
32. Egbe AC, Miranda WR, Mehra N, Ammash NM, Missula VR, Madhavan M, et al. Role of QRS Fragmentation for Risk Stratification in Adults With Tetralogy of Fallot. *J Am Heart Assoc [Internet].* 2018 Dec 18 [cited 2021 Jan 9];7(24). Available from: <https://www.ahajournals.org/doi/10.1161/JAHA.118.010274>
33. Berul CI, Hill SL, Geggel RL, Hijazi ZM, Marx GR, Rhodes J, et al. Electrocardiographic Markers of Late Sudden Death Risk in Postoperative Tetralogy of Fallot Children. *J Cardiovasc Electrophysiol.* 1997 Dec;8(12):1349–56.
34. Papagiannis JK. Postoperative Arrhythmias in Tetralogy of Fallot. *Hell J Cardiol.* 2005 Oct;46(6):402–7.
35. Roos-Hesselink J, Perlroth MG, McGhie J, Spitaels S. Atrial arrhythmias in adults after repair of tetralogy of Fallot. Correlations with clinical, exercise, and echocardiographic findings. *Circulation.* 1995 Apr 15;91(8):2214–9.

36. Harrison DA, Siu SC, Hussain F, MacLoughlin CJ, Webb GD, Harris L. Sustained atrial arrhythmias in adults late after repair of tetralogy of fallot. *Am J Cardiol.* 2001 Mar;87(5):584–8.
37. Garson A, Randall DC, Gillette PC, Smith RT, Moak JP, McVey P, et al. Prevention of sudden death after repair of tetralogy of Fallot: treatment of ventricular arrhythmias. *J Am Coll Cardiol.* 1985 Jul;6(1):221–7.
38. Cullen S, Celermajer DS, Franklin RC, Hallidie-Smith KA, Deanfield JE. Prognostic significance of ventricular arrhythmia after repair of tetralogy of Fallot: a 12-year prospective study. *J Am Coll Cardiol.* 1994 Apr;23(5):1151–5.
39. Waijen SA, Liu PP, Ross BL, Williams WG, Webb GD, McLaughlin PR. Serial follow-up of adults with repaired tetralogy of Fallot. *J Am Coll Cardiol.* 1992 Aug;20(2):295–300.
40. Liang X, Cheung EW, Wong SJ, Cheung Y. Impact of right ventricular volume overload on three-dimensional global left ventricular mechanical dyssynchrony after surgical repair of tetralogy of Fallot. *Am J Cardiol.* 2008 Dec 15;102(12):1731–6.
41. Piazza L, Chessa M, Giamberti A, Bussadori CM, Butera G, Negura DG, et al. Timing of pulmonary valve replacement after tetralogy of Fallot repair. *Expert Rev Cardiovasc Ther.* 2012 Jul;10(7):917–23.
42. Kjaergaard J, Iversen KK, Akkan D, Møller JE, Køber LV, Torp-Pedersen C, et al. Predictors of right ventricular function as measured by tricuspid annular plane systolic excursion in heart failure. *Cardiovasc Ultrasound.* 2009 Nov 4;7(1):51.
43. López-Candales A, Rajagopalan N, Saxena N, Gulyasy B, Edelman K, Bazaz R. Right ventricular systolic function is not the sole determinant of tricuspid annular motion. *Am J Cardiol.* 2006 Oct 1;98(7):973–7.
44. Núñez-Gil IJ, Rubio MD, Cartón AJ, López-Romero P, Deiros L, García-Guereta L, et al. Determination of normalized values of the tricuspid annular plane systolic excursion (TAPSE) in 405 Spanish children and adolescents. *Rev Esp Cardiol.* 2011 Aug;64(8):674–80.
45. Di Salvo G, Pacileo G, Rea A, Limongelli G, Baldini L, D’Andrea A, et al. Transverse strain predicts exercise capacity in systemic right ventricle patients. *Int J Cardiol.* 2010 Nov 19;145(2):193–6.
46. Kavey R-EW, Thomas FD, Byrum CJ, Blackman MS, Sondheimer HM, Bove EL. Ventricular arrhythmias and biventricular dysfunction after repair of tetralogy of Fallot. *J Am Coll Cardiol.* 1984 Jul;4(1):126–31.
47. Daliento L, Rizzoli G, Menti L, Baratella MC, Turrini P, Nava A, et al. Accuracy of electrocardiographic and echocardiographic indices in predicting life threatening ventricular arrhythmias in patients operated for tetralogy of Fallot. *Heart.* 1999 Jun 1;81(6):650–5.

48. Kuzevska-Maneva K, Kacarska R, Gurkova B. Arrhythmias and conduction abnormalities in children after repair of tetralogy of Fallot. *Vojnosanit Pregl.* 2005;62(2):97–102.
49. Niezen RA, Helbing WA, van der Wall EE, van der Geest RJ, Rebergen SA, de Roos A. Biventricular systolic function and mass studied with MR imaging in children with pulmonary regurgitation after repair for tetralogy of Fallot. *Radiology.* 1996 Oct;201(1):135–40.
50. Vliegen HW, van Straten A, de Roos A, Roest AAW, Schoof PH, Zwinderman AH, et al. Magnetic Resonance Imaging to Assess the Hemodynamic Effects of Pulmonary Valve Replacement in Adults Late After Repair of Tetralogy of Fallot. *Circulation.* 2002 Sep 24;106(13):1703–7.
51. Kalman Jonathan M., VanHare George F., Olgin Jeffrey E., Saxon Leslie A., Stark Stephen I., Lesh Michael D. Ablation of ‘Incisional’ Reentrant Atrial Tachycardia Complicating Surgery for Congenital Heart Disease. *Circulation.* 1996 Feb 1;93(3):502–12.
52. Steeg CN, Krongrad E, Davachi F, Bowman FO, Malm JR, Gersony WM. Postoperative left anterior hemiblock and right bundle branch block following repair of tetralogy of Fallot. Clinical and etiologic considerations. *Circulation.* 1975 Jun;51(6):1026–9.
53. Wolff GS, Rowland TW, Ellison RC. Surgically induced right bundle-branch block with left anterior hemiblock. An ominous sign in postoperative tetralogy of Fallot. *Circulation.* 1972 Sep;46(3):587–94.
54. Watt TB, Pruitt RD. Focal Lesions in the Canine Bundle of His: THEIR EFFECT ON VENTRICULAR EXCITATION. *Circ Res.* 1972 Oct;31(4):531–45.
55. Jonsson H, Ivert T, Brodin LA, Jonasson R. Late sudden deaths after repair of tetralogy of Fallot. Electrocardiographic findings associated with survival. *Scand J Thorac Cardiovasc Surg.* 1995;29(3):131–9.



# **APPENDIX**



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम  
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM  
Thiruvananthapuram - 695 011, Kerala, India  
(An Institute of National Importance under Govt. of India)

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**Institutional Ethics Committee**  
(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1350/FEBRUARY-2019

04.06.2019

**Dr. Karthik R**  
Resident  
Department of Cardiology  
SCTIMST, Thiruvananthapuram

Dear Dr. Karthik,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "ARRHYTHMIAS IN POST-SURGICAL TETRALOGY OF FALLOT INDIVIDUALS (IEC/1350)" on 16<sup>th</sup> February, 2019.

The following documents were reviewed:

Original submission

1. Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 28.11.2018 with checklist
2. TAC Approval Letter
3. IEC Application Form
4. Project Proposal
5. Proforma
6. Patient Information Sheet and Consent Form in English and Malayalam
7. CV of Principal Investigator and Co-Principal Investigators

Revised submission

1. Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 15.05.2019 with checklist
2. TAC Approval Letter
3. IEC Application Form
4. Project Proposal
5. Proforma
6. Assent Form
7. Patient Information Sheet and Consent Form in English and Malayalam
8. CV of Principal Investigator and Co-Principal Investigators

The following members of the Ethics Committee were present at the meeting held on 16<sup>th</sup> February, 2019 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Dr. Harikrishna Varma PR	Ph.D( Materials Science)	Male	Medical Technology	Yes
5.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
6.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
7.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
8.	Dr. P. Manickam	BSMS, MSc (Epid),PhD	Male	Health Science Expert/ Social Scientist	No
9.	Mr. Satheesh Chandran	MSW, PGDPM	Male	Lay person/ NGO/ Social Scientist	No
10.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
11.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

#### IEC Decision

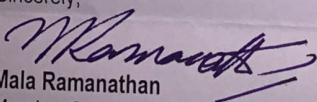
The IEC approved the conduct of the study in the present form.

#### Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

  
**Mala Ramanathan**  
 Member Secretary, IEC

# PROFORMA

## Arrhythmias in Post-Surgical Tetralogy of Fallot Patients.

**Patient No:**

Age: Years

Sex: M/F

**Follow up Date:**

H. No:

Home Town:

Contact No:

Height:

Weight:

BSA:

Diagnosis:

Situs S / I / A

Cardiac position D/ L / M

Ventricular function

Pulmonary Regurgitation

Surgery date

Comorbidities:

Current Medications:

### CLINICAL FEATURES

- NYHA Class
- Vitals HR                      BP                      SpO2
- Palpitations/ Presyncope/ Syncope
- Academics    Poor/ Fair/ Good                      Education                      Profession
- Married?

### ECG Findings:

- Rhythm :
- Heart Rate :
- QRS Duration:
- Axis
- Pre OP ECG:
  - QTc
  - QT dispersion
  - QRS duration
- Post OP ECG
  - QTc
  - QRS duration

### Echo Findings:

- Principal diagnosis
- EF
- LV Dimensions
- RV Dimensions                      EF                      TAPSE
- Pulmonary regurgitation



**SREE CHITRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND  
TECHNOLOGY, TRIVANDRUM  
PATIENT INFORMATION SHEET**

**TITLE: Arrhythmias in Post-Surgical Tetralogy of Fallot Patients.**

**Name of Investigators:**

Dr. Karthik R, Dr Dr. K.K.Narayanan Namboodiri, Dr. K. M. Krishnamoorthy

Dear Patient/Parent

We welcome you and thank you for your interest in your/ your child's participation in this research project titled "Arrhythmias in Post-Surgical Tetralogy of Fallot Patients". We hope to include 500 people from this hospital in the study. Before you/your child participate in this study, it is important for you to understand why this research is being carried out. This form will provide you all the relevant details of this research. It will explain the nature, the purpose, the benefits, the risks, the discomforts, the precautions and the information about how this project will be carried out. It is important that you read and understand the contents of the form carefully. This form may contain certain scientific terms and hence, if you have any doubts or if you want more information, you are free to ask the study personnel or the contact person mentioned below before you give your consent and also at any time during the entire course of the project.

**What are Arrhythmias in post-surgical Tetralogy of Fallot patients?**

Arrhythmias (irregular heart beat) can occur in individuals who have had surgery for Tetralogy of fallot. This can be due to the scar on the heart after the surgery which causes an electrical short circuit in the heart leading to an irregular heartbeat. This can cause palpitations(sensation of a fast heart beats) , presyncope (giddiness, blurring of vision) or syncope( Loss of consciousness).

**What does the present study involve?**

The records of the previous operation that you/your child has undergone will be collected from the hospital database. You will be contacted by phone/ by mail to visit the hospital on a particular day. You/ yourself along with your child will usually come in to hospital on the day of appointment. A specialist doctor will explain the proposed study design to you and ask you to sign the consent form to confirm that you understand the procedure and agree to go ahead with it. Please ask any questions you want.

Following enrolment into the study, you/your child will undergo the following tests- usually done as part of standard protocol and routine follow up evaluation:

- Electrocardiogram
- Echocardiogram
- Any other test deemed necessary as part of evaluation

**How long does it take?**

The hospital visit will be a routine consultation, and the tests done will be part of routine follow up. This may take upto 2-3 hours. Please be prepared to be in the hospital OPD during that time.

**WHAT ARE THE RESPONSIBILITIES OF PARTICIPANTS?**

Your decision to participate/to allow your child to participate in this study is voluntary, your own personal choice. You may choose not to continue at any time, for any reason, without notice.

**WHAT ARE THE EXPECTED RISKS FOR THE PARTICIPANTS?**

The study involves collection of previous data from case records, and a follow up evaluation to assess the arrhythmias that can occur in post surgical Tetralogy of fallot individuals. There will be no risks for the participants because of participation in the study. They will be managed according to the hospital protocol. No specific intervention will be done.

**WHAT ARE THE EXPECTED BENEFITS OF THE RESEARCH TO THE PARTICIPANTS?**

The participants are evaluated for any history suggestive of arrhythmia. All patients will undergo a detailed evaluation which can be beneficial in assessing their risk for future arrhythmia and can help in deciding early treatment or intervention if required. Data from this study may be helpful in identifying a sub group of patients who underwent surgical correction of tetralogy of fallot who are at an increased risk of morbidity or mortality from arrhythmias. This can help clinicians in guiding their decisions and define the best course of management in these patients

**WILL PARTICIPANTS BE COMPENSATED FOR PARTICIPATION IN THIS TRIAL?**

You will not be paid for participation in the study.

**WILL MINE/MY CHILD'S PARTICIPATION IN THIS STUDY BE KEPT CONFIDENTIAL?**

All records of your/your child's study will be kept confidential. Your child's personal identity will not be revealed in any publication or release of results. Study records will be kept indefinitely for analysis and follow-up.

**CAN I WITHDRAW FROM THE STUDY AT ANY TIME DURING THE STUDY PERIOD?**

Yes, you can. Your decision will not affect your regular medical care.

**IF THERE ARE ANY NEW FINDINGS / INFORMATION, WOULD I BE INFORMED?**

Yes.

**WHAT HAPPENS IN CASE OF A STUDY RELATED INJURY?**

There will be no study related injury.

**IS THERE ANY ALTERNATIVE TO THE TREATMENT MENTIONED?**

Not applicable.

If you have any further questions, please ask: Dr. Karthik R (Principal investigator), Senior Resident, Department of Cardiology (Email: [karthikr@sctimst.ac.in](mailto:karthikr@sctimst.ac.in) Ph No: 9843447652)

**For any technical clarifications, please contact** Study Independent Contact Person Dr. K .Shivakumar, Ph no:0471-2524593

# CONSENT FORM

**Title of the study:**

**Arrhythmias in Post-Surgical Tetralogy of Fallot Patients**

**Participant's name:**

**Age (in years):**

I \_\_\_\_\_, son/daughter/husband/wife of  
\_\_\_\_\_ declare that (Please tick boxes)

- I have read the above information provided to me regarding the study. [ ]
- I have clarified any doubts that I had. [ ]
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal Rights [ ]
- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access. [ ]
- I understand that my identity will not be revealed in any information released to third parties or in publication of study results. [ ]
- I voluntarily agree to take part in this study [ ]
- I understand that participation in the study means that I am willing to undergo the said procedure as already explained and my health records shall be accessed by the investigators for the purpose of the study. [ ]
- I understand that I do not have to bear any extra expense for the purpose of this study. No financial support will be provided to me for participation in the study. [ ]
- I have been provided with the contact numbers of the principle investigator, in case I want to know more about the study and participants rights [ ].
- I have received a copy of this signed consent form [ ]

Name:

Signature:

Name of witness:

Signature:

Relation to participant:

## Person Obtaining Consent

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her \_\_\_\_\_, in nontechnical terms, all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and all questions asked were answered.

Name:

Signature:

Date:

Place:SCTIMST, Thiruvananthapuram

Principal investigator

A rectangular box containing a handwritten signature in blue ink that reads "Karthik R".

Dr.Karthik R

Shristy Hostel, Sree Chitra Quarters

Trivandrum

Mobile. 09843447652

Date – 3-12-2018

Study Independent Contact Person

Dr. K Shivakumar

0471-2524593

## Informed Consent (Assent form)

**Participant's name:**

**Date of Birth / Age (in years):**

I \_\_\_\_\_,  
son/daughter of \_\_\_\_\_ (Please tick  
boxes) • declare that

• I have read the above information provide to me regarding the study: **Arrhythmias in Post-Surgical Tetralogy of Fallot Patients**. And have clarified any doubts that I had. [ ]

• I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]

• I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]

• I understand that my identity will not be revealed in any information released to third parties or published [ ]

• I voluntarily agree to take part in this study [ ]

• I received a copy of this signed consent form [ ]

Name:

Signature :

Signature of the

Father/Mother/Relative: Name of the

Father/Mother/Relative: Date:

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

\_\_\_\_\_  
Name and Signature of Person Obtaining Consent



























Heiter Details	Min HR	Max HR	Avg HR	VPC BURDEN(%)	APC BURDEN(%)	NSVT	NSVT RUNS	PAUSE	MIN	RVEDVI	RVEDVI	DEF	RVEF	PR(%)	LGE	MI details	EPS	EPS Details	SACT	Antegrade study	RETROGRADE STUDY	VT INDUCTION	Mortality	Mortality(Excluding therapy)	Mortality(pericardial)	Mortality date	Monthly Details	MORTALITY DETAILS	Residual VSD	Medications	Other
																						0	0	0							
Normal	48	132	66	0	0	0	0	1.5														0	0	0				1		RESIDUAL VSD- LOST TO FOLLOW UP	
																						0	0	0							
VE, NSVT	52	147	75	37	0	1	2340	1.7														0	0	0						advised review	
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Normal	45	128	63	0	0	0		1.4														0	0	0							
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