LONG-TERM OUTCOMES OF CONGENITALLY CORRECTED TRANSPOSITION OF GREAT ARTERIES WITH INTACT VENTRICULAR SEPTUM IN A TERTIARY CARE CARDIAC CENTRE IN SOUTH INDIA

Dr. Malla. Phanindra

DM CARDIOLOGY

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SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

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A THESIS SUBMITTED BY

Dr. Malla. Phanindra

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM.

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE AWARD OF

DM CARDIOLOGY

2023

DECLARATION BY THE STUDENT

CERTIFICATE

I, Dr. Malla. Phanindra, hereby certify that I had personally carried out the work depicted in the thesis titled, "**LONG-TERM OUTCOMES OF CONGENITALLY CORRECTED TRANSPOSITION OF GREAT ARTERIES WITH INTACT VENTRICULAR SEPTUM IN A TERTIARY CARE CARDIAC CENTRE IN SOUTH INDIA**".

No part of this thesis has been submitted for the award of any other degree or diploma prior to this date.

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Date 25/08/2023

CERTIFICATE BY THE RESEARCH GUIDE

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Division/Department: Cardiology

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The thesis entitled, "**Long-Term Outcomes Of Congenitally Corrected Transposition Of Great Arteries With Intact Ventricular Septum In A Tertiary Care Cardiac Centre In South India**" was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

*Clearance was obtained from the Institutional Ethics Committee / Institutional Animal Ethics / Institutional Committee for Stem Cell Research / Other appropriate committees (if any, specify) for carrying out the study.

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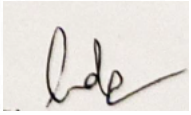

Signature
Dr. Deepa. S. Kumar

Date:21-08-2023

APPROVAL OF THE THESIS

The thesis entitled

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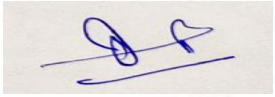

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LIST OF ABBREVIATIONS

S No	Abbreviation	Full Form
1	ccTGA	Congenitally corrected transposition of great arteries.
2	AV	Atrioventricular
3	VA	Ventriculoarterial
4	MV	Mitral valve
5	mLV	Morphologic Left ventricle
6	TV	Tricuspid valve
7	mRV	Morphologic Right ventricle
8	Ao	Aorta
9	PA	Pulmonary artery
10	IVS	Intact ventricular septum
11	DSO	Double Switch Operation
12	CHB	Complete heart block
13	LVOT	Left ventricular outflow
14	RVOT	Right ventricular outflow
15	CHF	Congestive heart failure
16	LVOTO	Left ventricular outflow obstruction
17	MRI	Magnetic resonance imaging
18	LGE	Late gadolinium enhancement
19	LVEF	Left ventricle ejection fraction
20	CT	Computed tomography

21	PVR	Pulmonary vascular resistance
22	AVVR	Atrioventricular valve regurgitation
23	CRT	Cardiac resynchronisation therapy
24	CSP	Conduction system pacing
25	3D	3 dimensional
26	CS	Coronary sinus
27	D-TGA	D-Transposition of great arteries
28	PAB	Pulmonary artery banding
29	VSD	Ventricular septal defect
30	ASO	Arterial switch operation
31	ECG	electrocardiogram
32	TAPSE	Tricuspid annular plane systolic excursion
33	FAC	Fractional area change
34	IQR	Inter quartile range
35	SD	Standard deviation
36	LC	Levocardia
37	DC	dextrocardia
38	MC	Mesocardia
39	LRTI	Lower respiratory tract infection
40	PPI	Permanent pacemaker implantation

"LONG-TERM OUTCOMES OF CONGENITALLY CORRECTED TRANSPOSITION OF GREAT ARTERIES WITH INTACT VENTRICULAR SEPTUM IN A TERTIARY CARE CARDIAC CENTRE IN SOUTH INDIA".

SYNOPSIS

BY

Dr. Malla. Phanindra

for DM CARDIOLOGY

of

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

SYNOPSIS

BACKGROUND: ccTGA is a congenital heart disease characterised by Atrioventricular discordance and ventriculoarterial discordance. ccTGA might be associated with ventricular septal defect and Pulmonary stenosis. The management of ccTGA with intact ventricular septum is controversial. Some prefer medical management, and some prefer Double switch operation. The main aim of the study is to study the outcomes of patients with ccTGA with intact ventricular septum. The main issues in ccTGA are a rarity, uncertain natural history, and heterogeneity of associated lesions.

METHODS: A single-centre retrospective analysis of all patients diagnosed with ccTGA with intact ventricular septum was reviewed. Primary objectives included Systemic ventricular dysfunction, systemic valvular regurgitation, and death. Secondary objectives include the clinical profile of the patients and the incidence of Complete Heart block, and the type of interventions and outcomes of the patients. The demographic data like age and gender, initial presentation, investigations like ECG, complete echo diagnosis, cardiac position, situs and associated anomalies were collected. Right ventricular function and Tricuspid regurgitation were collected at the initial and last follow-up visits.

RESULTS: The median age of diagnosis was 11 years (2.9-32.3). The cohort showed a majority male population. The most common position and Situs are Situs Solitus and

Levocardia (n-64%), followed by Situs inversus and dextrocardia (n-14%). Around 36% are incidentally detected. About 40% of the patients had more than moderate tricuspid regurgitation, which increased to 54% on follow-up. About 20 % had RV dysfunction at baseline; on follow-up, incidence increased to 35%. The median follow-up period was five years (2-14). The incidence of Complete heart block was 34%, and three patients were noted to have Atrial fibrillation. PA banding was done in 8 patients, and one underwent a Double switch operation. Four patients underwent tricuspid valve interventions. Mortality was seen in 8 patients, and 19 patients were lost to follow-up. Four patients underwent CRT, and there was an improvement in the functional status of the patients.

CONCLUSIONS: RV dysfunction was higher in patients with ccTGA with an intact ventricular septum. Over half of the patients developed more than moderate Tricuspid regurgitation on follow-up. The incidence of CHB was high due to the abnormality of conduction tissue in ccTGA. PA banding can be used as destination therapy for some patients with Moderate-Severe AVVR. CRT could be a better option for patients requiring pacemakers for CHB having ventricular dysfunction.

1. INTRODUCTION

Congenitally corrected Transposition of Great arteries (ccTGA) is a congenital heart disease characterised by atrioventricular (AV) discordance and ventriculoarterial (VA) discordance (Filippov et al., 2016; Thomas P. Graham et al., 2000; Wallis et al., 2011). It is associated with confusing nomenclature. Initially, it was called Double discordance or isolated ventricular inversion, or l-transposition. ccTGA is an anomaly characterised by cardiovascular connections in which the vena cavae connect to the right atrium, which empty through the mitral valve (MV) into the morphologic left ventricle (mLV). The mLV ejects into a discordantly connected pulmonary artery (PA) (Fig.). The left atrium receives blood from the pulmonary veins, emptying through the tricuspid valve (TV) with the morphologic right ventricle (mRV), which ejects into the aorta (Fig.). These atrioventricular (AV) and ventriculoarterial (VA) connections occur most commonly in the setting of situs solitus but can also be seen with situs inversus.

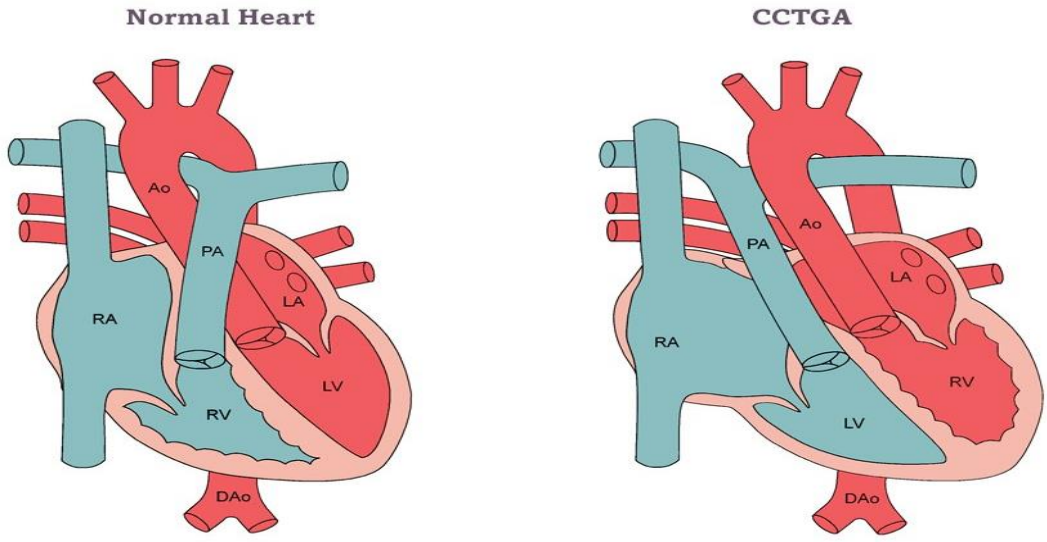


Figure-1-Diagrammatic representation of Normal Heart and ccTGA

In ccTGA, AV and VA discordance affects Pulmonary venous blood reaching the Aorta (Ao) and Systemic venous blood going to the Pulmonary artery(PA). However, with time the clinical course and hemodynamics become abnormal, even in patients without associated cardiac defects (Jatene et al., 1976).

Management of ccTGA with intact ventricular septum (IVS) is still controversial. Some centres prefer to continue to offer medical management, maintaining mRV as a systemic ventricle. In some patients, there is an increased risk of the development of Complete Heart block, Tricuspid regurgitation, and RV dysfunction on follow-up. In some centres, patients will undergo a Double switch Operation (DSO) in which mLV is made a systemic ventricle with prior LV training. Patients who develop progressive RV dysfunction and worsening tricuspid regurgitation are offered DSO with initial LV training. However, some patients may develop mLV dysfunction after DSO when the left ventricle cannot handle the systemic pressures.

Due to the condition's rarity, minimal data is available about the patients diagnosed with ccTGA with an intact ventricular septum. Some studies advocate medical management, and some centres support early Double switch operation in which LV is maintained as the systemic ventricle.

As the management is still controversial and there is limited data, our study adds to the existing literature about the outcomes of ccTGA with IVS.

PERTINENCE OF THE STUDY:

- Very few studies are available about the outcomes of the Congenitally corrected Transposition of Great Arteries with the Intact ventricular system.
- There is no data regarding the incidence of RV dysfunction, Complete Heart block, and mortality in patients with ccTGA with IVS from India.

2. AIMS AND OBJECTIVES

- To study the long-term outcomes in patients with congenitally corrected transposition of the great arteries (cc TGA) with an intact ventricular septum.

OBJECTIVES:

- The study's primary objective is the incidence of Right ventricular Dysfunction and Tricuspid regurgitation and mortality.
- The secondary objectives include the patient's clinical profile, the incidence of Complete Heart block (CHB), and the type of interventions and outcomes of the patients.

3. REVIEW OF LITERATURE

ccTGA is a congenital heart disease characterised by AV discordance and VA discordance. It is an uncommon disease with an incidence of about 0.03 per 1000 live births, which constitutes 0.4% of congenital heart diseases and 4% of conotruncal defects. (Canfield et al., 2006; Ferencz et al., 1985) The exact aetiology of ccTGA remains unclear, though there are some associations with genetic factors and maternal exposure to specific teratogens during fetal development. Embryologically the primitive cardiac tube gets anchored at one end by the sinus venosus and at the other end by the truncus arteriosus and loops to the left (l-loop) in ccTGA, not to the right (d-loop) as in the normal heart (7). This abnormal looping results in morphologic LV to the right and mRV to the left. Further twisting results in a superior to the inferior relationship of RV to LV. Another necessary consequence of l-looping is the orientation of the interatrial septum and interventricular septum. The right-sided AV valve has anatomic features similar to the mitral valve with two papillary muscles and is not attached to the interventricular septum. The left-sided AV has similar features to the tricuspid valve, which is septophilic and often malformed.

Patients with ccTGA are prone to develop left ventricular outflow (LVOT) obstruction as it is deeply wedged between right and left AV valves. The aortic valve is left and anterior to the Pulmonary valve. ccTGA is associated with Ventricular septal defects, LVOT obstruction, and left AV valve abnormalities. TV dysplasia is common and may occur with or without displacement of the septal or posterior leaflets of the TV (8). Coronary anatomy is important as it is essential for planning surgery.

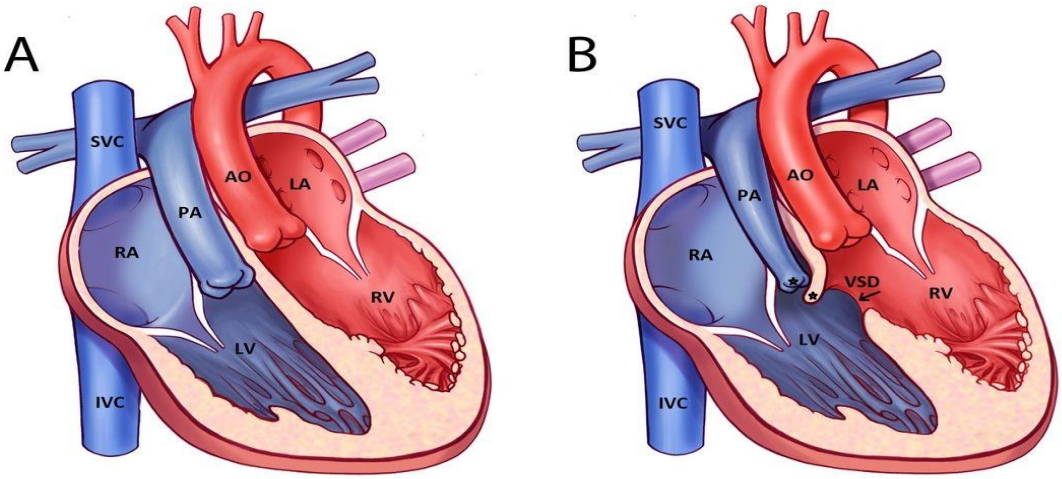


Figure-2 A. ccTGA with intact ventricular septum B. ccTGA with VSD and LVOT obstruction

The coronary arterial pattern in ccTGA is coronary artery ventricular concordance in which coronaries arise from posterior facing sinuses and distribute in a mirror image of normal (9). Various anomalies of coronary anatomy exist, like single coronary artery and main coronary crossing RVOT.

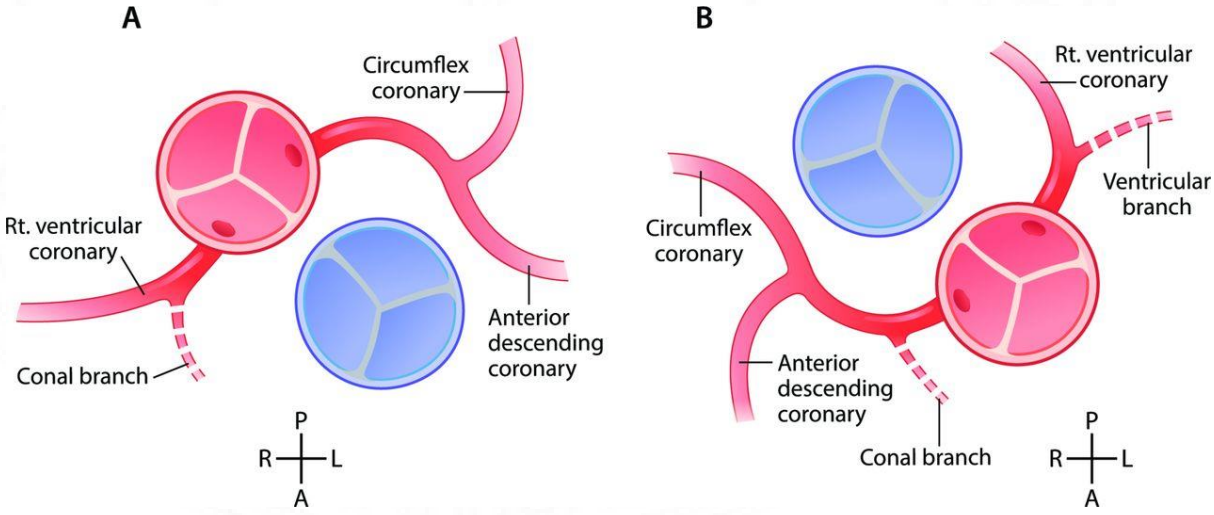


Fig-3 Coronary anatomy in A. Normal Heart B. ccTGA

The conduction system in ccTGA is abnormal. The sinoatrial node is normal and is related to the atrial situs. The Atrioventricular node is abnormal. It is classically described as two AV nodes: (a) a normally positioned posterior AV node at the apex of the triangle of Koch but with no AV bundle, and (b) an abnormal right anterior AV node giving rise to the penetrating AV bundle, upon which AV conduction depends. The bundle branches are in concordant association with the morphologic ventricles, the left bundle on the right, and the right bundle on the left side of the septum. The main cause of rhythm abnormalities in ccTGA is abnormal ventricular looping and septal malalignment.

Clinical recognition of ccTGA is delayed because many patients are symptom-free for decades. If patients develop symptoms, it might be most commonly due to Heart failure due to a failing ventricle and arrhythmia.

Right ventricular dysfunction and Tricuspid regurgitation:

Patients are more prone to develop RV dysfunction and Tricuspid regurgitation in the later part of life in the natural history of ccTGA(1,10,11). The tricuspid valve is frequently dysplastic and exposed to high RV systemic pressure, and becomes regurgitant. The RV is volume loaded from TR and working against systemic pressures. The causes for the development of RV dysfunction are intrinsic geometry, Fiber orientation, and lower coronary flow reserve. In one series of 40 patients with ccTGA, systemic RV dysfunction was almost always linked to long-standing TR and was the most important factor associated with poor outcomes (12).

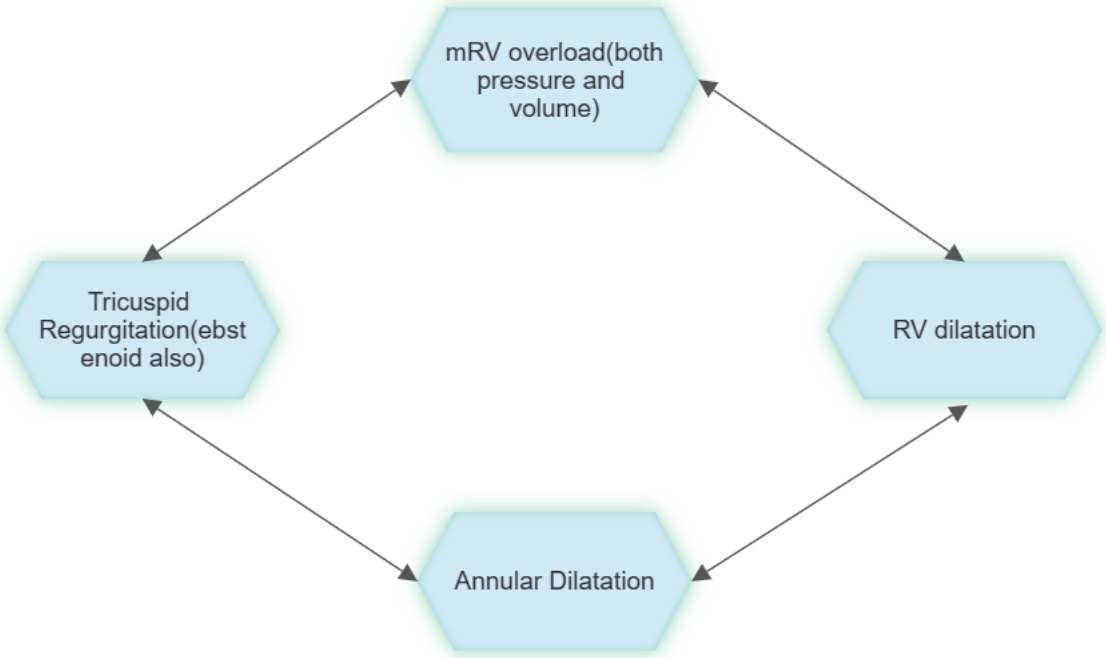


Fig 4 : Vicious cycle of Tricuspid regurgitation and RV dysfunction

Electrocardiographic features of ccTGA include normal P wave, which is positive in II, III, aVF, and negative in aVR. The activation of ventricles in ccTGA is abnormal. Normal ventricular activation takes place from left to right producing qR in V6 and rS in V1. Due to the more or less sagittal (left posterior to right anterior) ventricular septal orientation in ccTGA and inversion of the ventricular bundle branches, the sequence of initial activation is oriented from right to left, usually in a more superior and anterior direction(13). This results in qR in V1. In addition to the qR pattern, prominent Q waves are seen in II, III, and aVF. Second-degree and third-degree AV blocks are seen in some patients, and they might be presenting complaints in some patients. Complete AV block is present at birth in around 4 %, and 20-30% of patients develop Complete Heart block (CHB) in their lifetime(14,15).

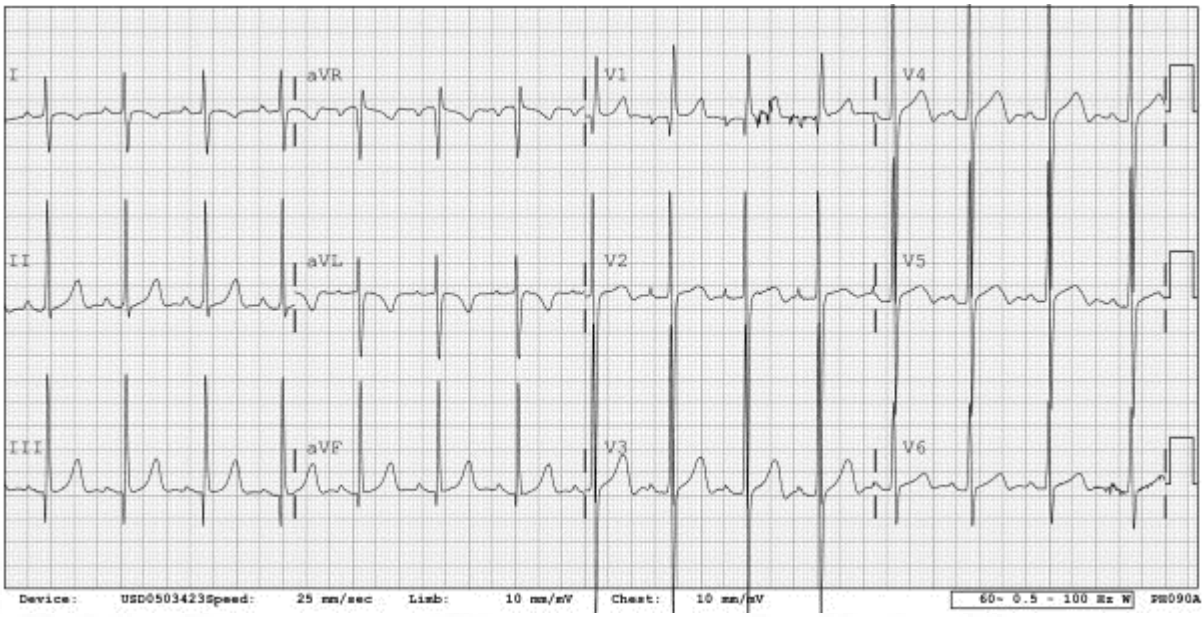


Fig-5 ECG showing qR pattern in V1 and large q waves in III, aVF

Chest radiographs in patients without associated defects will be normal except for the L-posed Aorta on the left Heart border. In patients with congestive heart failure (CHF) and TR and RV dysfunction, cardiomegaly is seen.

ECHOCARDIOGRAPHY:

The echocardiography of ccTGA begins with the determination of the situs and the position of the heart. By taking the subcostal view of the heart, the cardiac position can be determined. 25% of patients with ccTGA will demonstrate either dextrocardia or Mesocardia. The sub-costal view helps in the identification of Criss-cross ventricles and superior-inferior ventricles.

Identification of AV discordance can be identified by atrioventricular septum malalignment. The RV and LV can be identified by the morphology of the Atrioventricular valve and the morphology of the ventricles. RV can be determined by the Tricuspid valve with septal attachments, moderated band, and coarse

trabeculations (smooth surface of LV). Some of the patients are noted to have Ebstenoid malformation of the Left-sided AV valve. The parasternal long axis will give orientation to great arteries. Aorta is left and anterior to the Pulmonary artery in ccTGA. Other associated defects like Atrial septal and ventricular septal defects should be seen. Some of the patients are noted to have LVOTO. Coronary anatomy also can be studied with a careful focus on Ascending aorta. Most patients have coronary distribution (67%) corresponding to ventricles (16). Some of the patients are noted to have single coronaries.

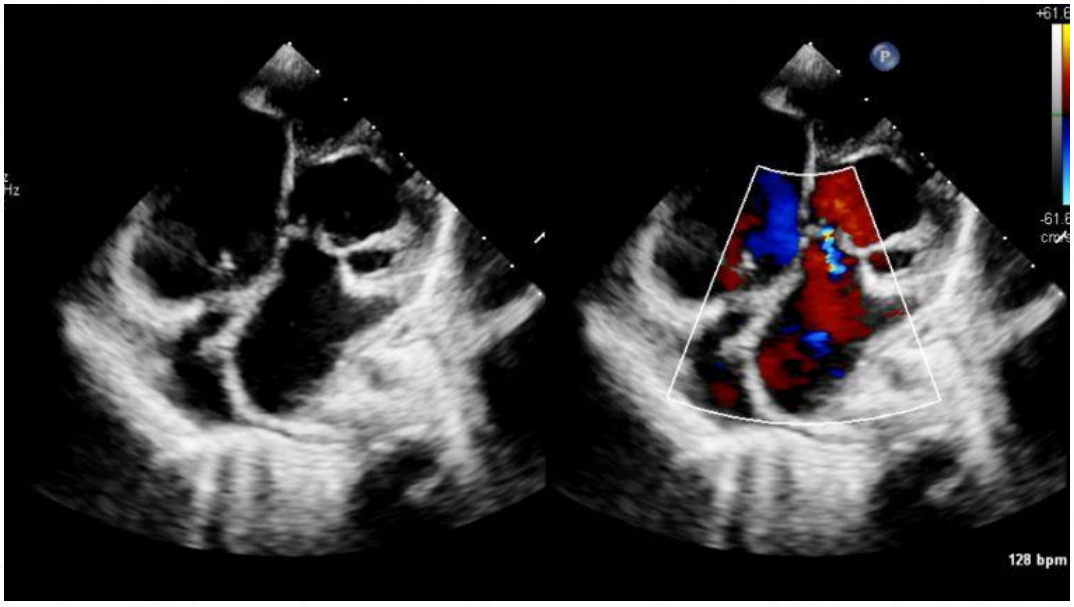


Fig 6 : Apical four-chamber view showing AV discordance with left-sided Tricuspid valve showing mild-moderate TR

MAGNETIC RESONANCE IMAGING(MRI): MRI can be used as a useful alternative tool for the anatomy of complex lesions. It also gives information on ventricular function, volumes and degree of valvular regurgitation. RV function can be better assessed by MRI, which shows a better correlation with other imaging modalities. RV fibrosis which can be detected by late gadolinium enhancement (LGE),

tells us the incidence of arrhythmias, RV dysfunction, and clinical outcomes. LV mass and LVEF post-PA banding can be assessed for adequate LV retraining. CT can be used as an alternative imaging modality in whom MRI is contraindicated. CT helps in better lineation of coronary anatomy.

ANGIOGRAPHY:

Invasive angiography helps in the assessment of hemodynamics and anatomical abnormalities. It also helps determine Pulmonary vascular resistance (PVR) in some cases where patients are noted to have severe AV valve regurgitation (AVVR). Precaution should be taken during catheterisation as patients are more prone to develop AV block during catheter manipulation. Left ventricular End diastole and LV function can be assessed by catheterisation for LV retraining.

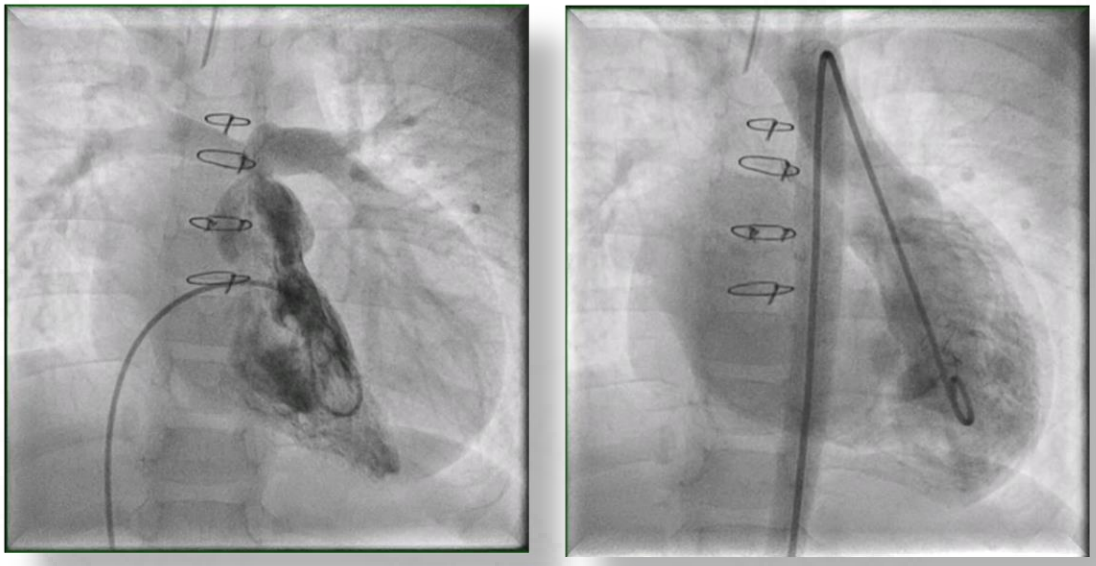


Fig 7 : RV and LV angiogram in AP view in a post-PA banding patient show Severe Left AVVR, L-posed Aorta, normal pulmonary arteries, and intact interventricular septum.

MANAGEMENT:

Management of ccTGA is controversial because the Fate of RV as a systemic ventricle is unpredictable. In some patients, RV dysfunction develops early and in some patients in the 4^{th}-6^{th} decade. Factors that determine RV dysfunction are unpredictable. Tricuspid regurgitation that develops might be due to malformation or due to RV dysfunction and is highly associated with the development of RV dysfunction and even worsens it.

The natural history is mainly influenced by associated lesions. A study by Graham et al. found that the incidence of RV dysfunction was lower in patients with intact ventricular septum when compared with related defects. However, both the groups develop RV dysfunction and Tricuspid regurgitation on follow-up(Thomas P. Graham et al., 2000).

Natural History	
AV Block	Birth to Death
Tricuspid Regurgitation	End of the first decade to Death
Arrhythmias	End of the third decade to Death
CHF	unpredictable
Increased Mortality Risk	Risk increases after the third decade

Table-1 Natural history of ccTGA (timing of development of complications)

Medical management mostly depends on the management of Heart failure with Diuretics, Afterload reducing agents, and Beta-blockers.

Permanent pacemaker implantation is needed in patients who develop Complete Heart block as CHB results in symptoms. In patients with ventricular dysfunction Cardiac Resynchronisation Therapy (CRT) or Conduction system pacing (CSP) can

be done(17). Performing CRT or CSP is difficult in patients with ccTGA because of varied coronary sinus anatomy and cardiac venous system anatomy. 3D Mapping of the conduction system is required to capture bundle branches adequately. In patients who underwent Anatomic repair, CS is difficult to access, and, in such conditions, epicardial pacing or a Hybrid approach can be tried.

Surgery:

Surgeries commonly performed in patients with ccTGA are either Physiological repair, Anatomical repair, Palliative procedures, or LV retraining. Physiological repair only corrects the associated defects and maintains RV as a systemic ventricle. Immediate surgical outcomes are good in physiological repair, but in the long term, the incidence of RV dysfunction and worsening of tricuspid regurgitation is seen. In a study by Hraska et al., the outcome of 123 patients with ccTGA of which 96 had a physiologic repair, had 5-year survival rates at 75% and 10-year at around 68%. Freedom from RV dysfunction was 88% at the end of 1 year, dropping to 43% at ten years. Similarly, the incidence of TV dysfunction after intracardiac repair was 9% at one year but rose to 48% at ten years (18).

Recommendations	Class
In symptomatic patients with Severe TR with preserved or mildly impaired systemic RV function.TV replacement is indicated.	I
In asymptomatic patients with severe TR and progressive systemic RV dilatation or mildly impaired RV systolic function	II a

Biventricular pacing should be considered in case of a complete AV block or more than 40 % pacing requirement.	II a
In symptomatic patients with Severe TR and more than mildly reduced EF, TV replacement can be considered.	II b

Table-2 Recommendation for interventions in ccTGA(copied from ESC)

A study by Prieto et al. concluded that TR was the single most important factor associated with poor outcomes and the development of RV dysfunction. (Prieto et al., 1998) Some studies have suggested early intervention for Tricuspid regurgitation results in delayed deterioration of RV function.

PA banding was used to train LV before anatomical repair. In a study by Kral Collars et al., the PA banding grade of tricuspid regurgitation came down after intervention which in turn helps improve RV function (19).In a study by Winlaw et al., there was no improvement in TR, but clinical improvement was identified (20). In a study by Shuhei Toba et al., significant cardiomyocyte hypertrophy was observed but lower capillary density in patients with ccTGA with IVS or D-TGA with IVS after PAB for retraining compared with normal control subjects. This finding suggests inadequate capillary growth is a significant reason for the incidence of mLV dysfunction after retraining or anatomic repair (21).

Factors that contribute to a decrease in TR after PA banding:

- Septal shift
- RV becomes less spherical
- Increased coaptation of tricuspid valve leaflets

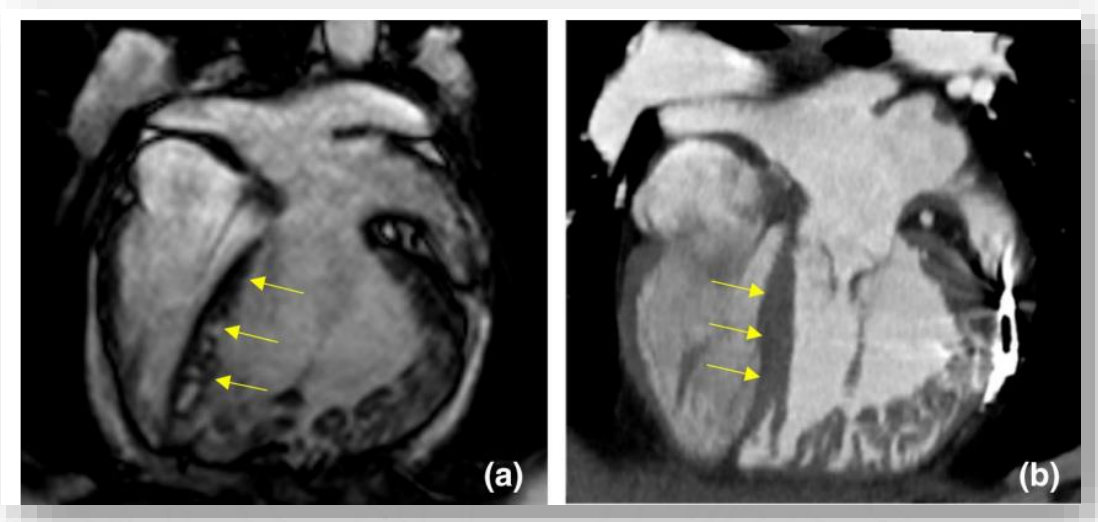


Fig 8 : Effect of PA banding on IVS a. Before PA banding b. After PA banding septal shift is observed

An anatomic repair is an approach in which mLV is made a systemic ventricle. It includes an atrial switch in the form of a Senning or Mustard. In patients with associated defects such as VSD or RVOT Senning+ Rastelli, an approach can be used, which includes placement of conduit from RV to PA and LV ejection through VSD to the aorta. In patients with normal pulmonary valves, Double Switch Operation (arterial switch+ atrial switch) can be done.

Complications of Anatomic repair include:

1. Atrial switch operation -sinus node dysfunction, baffle obstruction and baffle leaks, and supraventricular arrhythmias
2. Rastelli- Subaortic obstruction, Aortic regurgitation, conduit obstruction

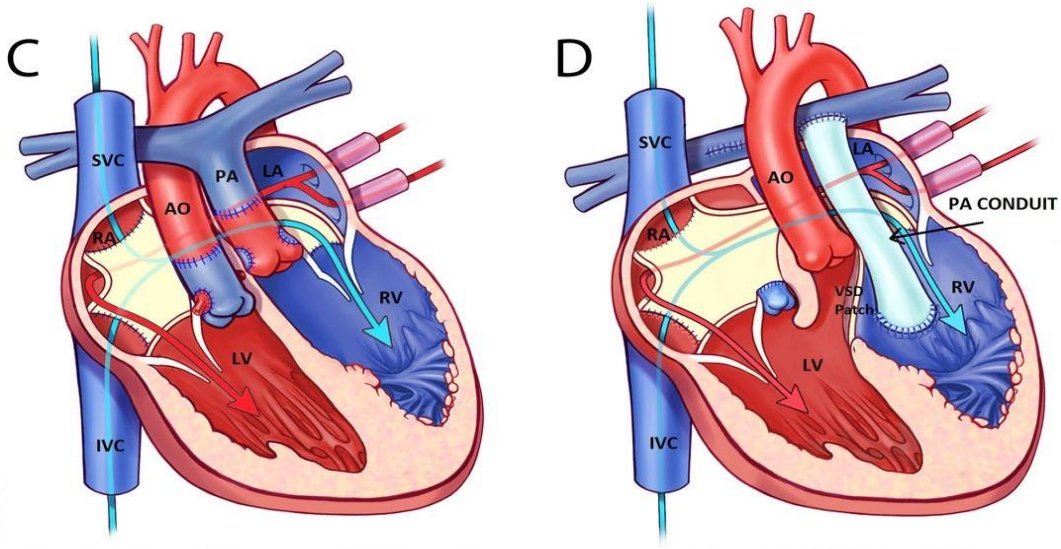


Fig 9 : C-Double switch operation D-Senning+ Rastelli

3. Arterial switch operation (ASO)-coronary artery obstructions, aortic valve incompetence, Pulmonary artery obstruction.

PA banding has been used to retrain the deconditioned LV. If done after two years of age, PA banding does not result in adequate LV training. Some patients develop LV dysfunction after PA banding. When successful, LV retraining is reported to require a median of 12 to 14 months of banding (20,22–25). The Criteria for successful retraining include LV pressure ≥70% to 85% systemic, LV mass/LV volume ratio >1.5, LV wall thickness or mass within normal limits for a systemic LV, and normal LV function after PA banding(20,26,27).

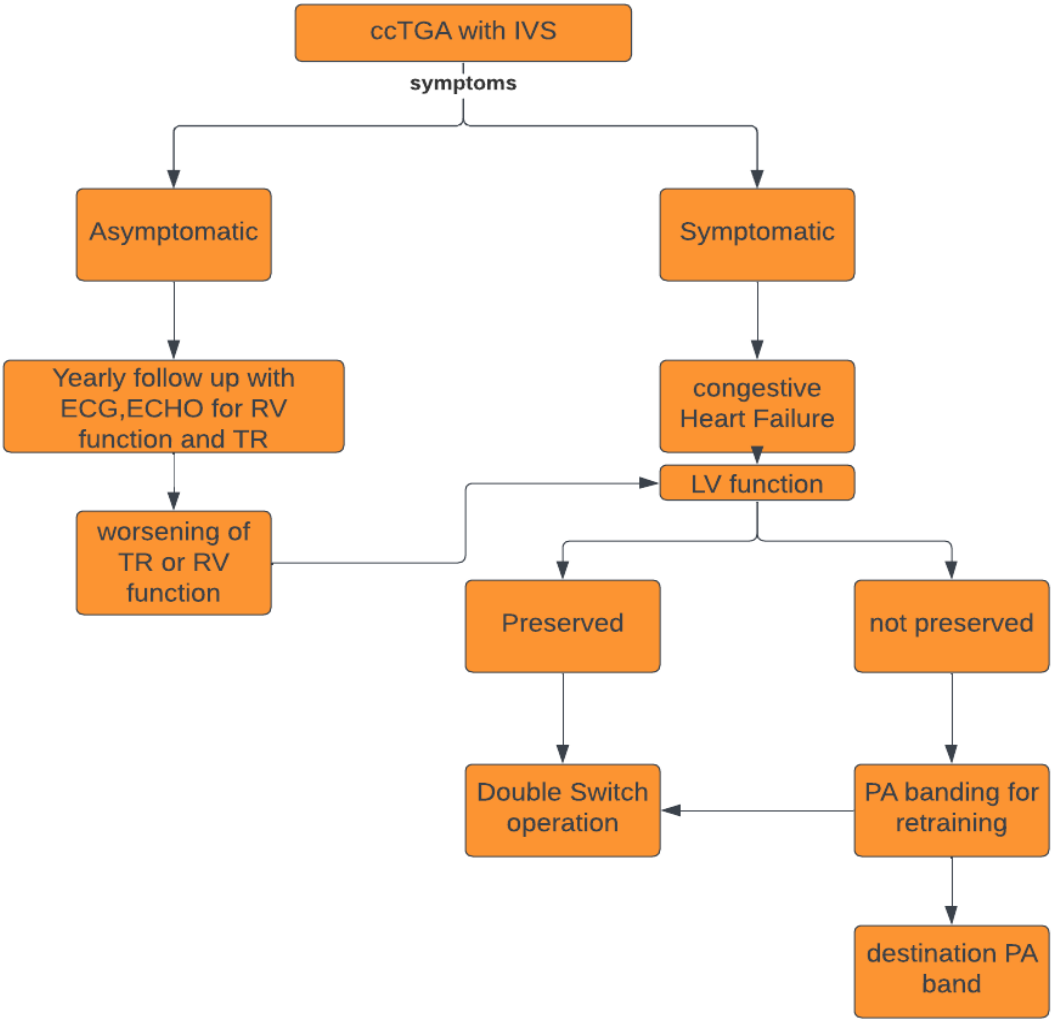


Fig 10: Flow chart showing management of ccTGA with intact ventricular septum

4. MATERIALS AND METHODS

Design: Retrospective observational study

Study Setting: Department of Cardiology, Sree Chitra Tirunal Institute of Medical Sciences and Technology (SCTIMST), Trivandrum.

Study period: from 01.06.2021 to 30.04.2023

Sample Size: The data was collected from Electronic Medical Records, Department of Cardiology of SCTIMST, starting from January 1990 to December 2022.

- INCLUSION CRITERIA-
    - Patients diagnosed with ccTGA with Intact ventricular septum who were registered with SCTIMST.
- EXCLUSION CRITERIA-
    - Patients with a diagnosis of ccTGA with other associated anomalies, such as VSD, were excluded

DATA COLLECTION AND PROCEDURE:

- The demographic data like age and gender, initial presentation, investigations like ECG, complete echo diagnosis, including cardiac position, situs and, associated anomalies, were collected
- Right ventricular function and Tricuspid regurgitation at the initial visit and last follow-up visit were collected
- Timing and outcome of surgery/ interventions were collected
- Study parameters: - age, gender, functional class at presentation
- Age at presentation and age at the definitive procedure.
- Associated lesions

- Rhythm abnormalities
- Timing of PA band and indications
- Type of surgery performed
- Any pacemaker implantations
- Any CRT implantations
- Assessment of RV and LV function, valvar regurgitation
- Length of Hospital stay
- Type of Tricuspid valve repair/replacement
- The outcome of the Senning / Arterial switch/Rastelli operation
- Follow-up Of Patients –Functional Class, Echocardiographic Parameters.
- Mortality And Systemic Ventricle Dysfunction

Echocardiography:

Routine echocardiography imaging, such as situs and position of the heart, is seen. The atrioventricular and Ventriculoarterial connections are examined. Tricuspid regurgitation is graded according to ASE guidelines.

Right ventricular function assessment was done using Tricuspid annular plane systolic excursion (TAPSE) and Right ventricular Fractional area change (RV FAC).RV function is divided into mild RV dysfunction and Severe RV dysfunction.

	TAPSE	**RV FAC**
Normal RV function	>17	>35
Mild RV dysfunction	15-17	31-35
Severe RV dysfunction	<15	<30

Table-3 : Quantification of RV function

STATISTICAL ANALYSIS

- Data was entered in MS Excel and analysed in SPSS V25.
- Descriptive statistics were represented with percentages for qualitative data, mean with standard deviation (SD), or Median with interquartile range (IQR) for quantitative data.
- Shapiro Wilk test was applied to find normality.
- The chi-square test and Fisher Exact test were applied for the comparison of proportions.
- Man-Whittney U test was applied for comparison between medians.
- $P<0.05$ was considered statistically significant.

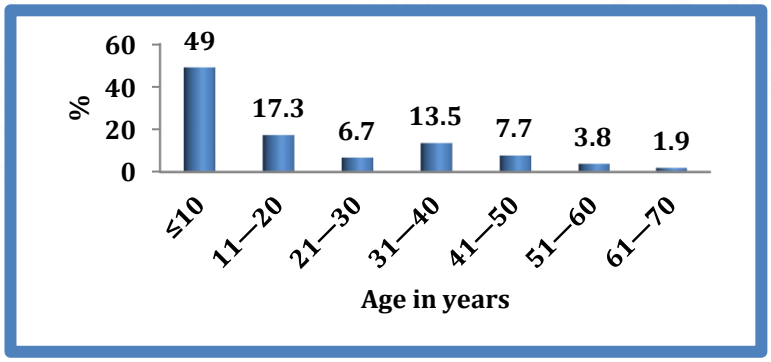
5. RESULTS

From 1990 to 2022,104 patients were diagnosed with ccTGA with Intact ventricular septum at our institute. The median age at the first presentation was 11 years (2.9-32.3 years). The duration of follow-up was 5 years (2-14 years). Around 49 percent of the study population presented to our hospital were below 10 years of age. Table-4 and fig -11 show the timing of the population's presentation.

Table-4:

Age	Frequency	%
≤10	51	49.0
11—20	18	17.3
21—30	7	6.7
31—40	14	13.5
41—50	8	7.7
51—60	4	3.8
61—70	2	1.9
Total	104	100.0

Fig-11

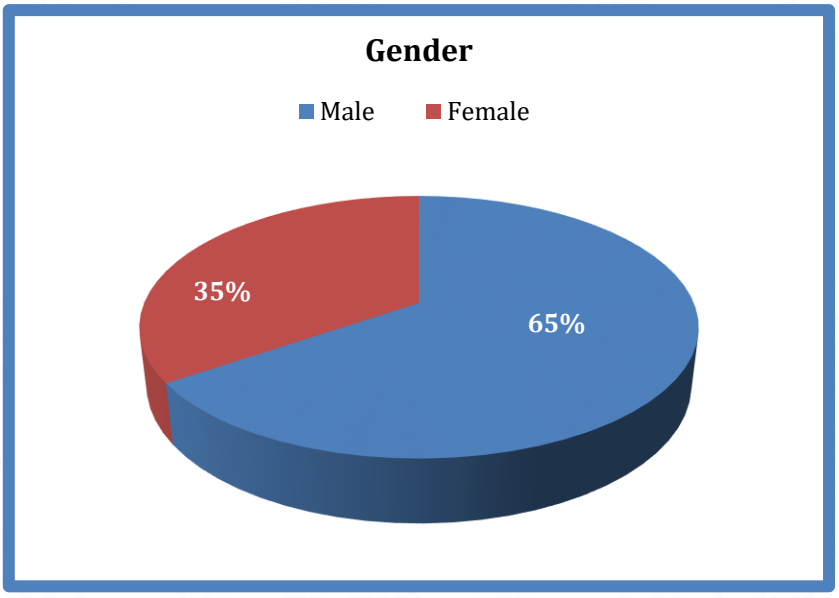


The gender distribution of the study population shows male predominance with around 65 percent. Table-5 and figure-12 show the gender distribution of the population.

TABLE-5

Gender	Frequency	%
Male	68	65.4
Female	36	34.6
Total	104	100.0

FIG-12



Most of the study cohort had Situs Solitus, Levocardia (n-67) followed by Situs Inversus, Dextrocardia seen in 18.3%. Table-6 and figure-14 show the distribution of position.

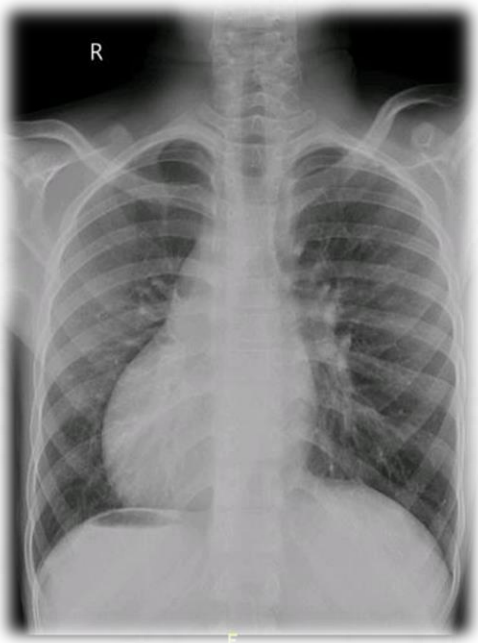


Fig:13-a CXR showing SI, DC

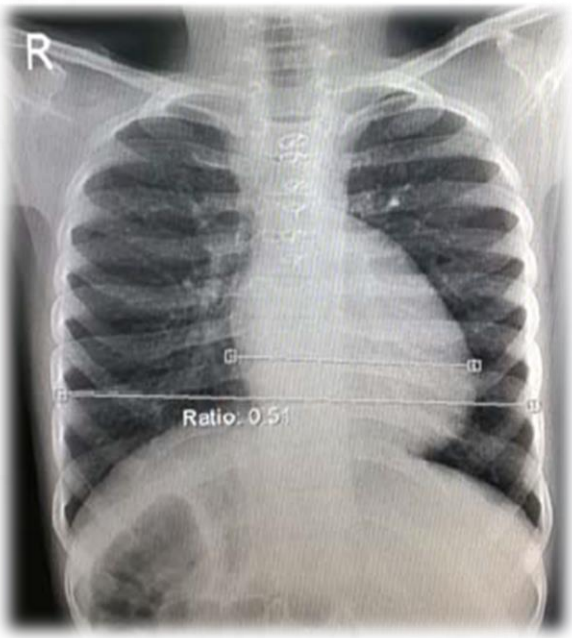


Fig:13-b CXR showing SI, LC

Table-6

POSITION	n
SS, LC	67
SS, DC	11
SS, MC	7
SI, LC	4
SI, MC	0
SI, DC	15

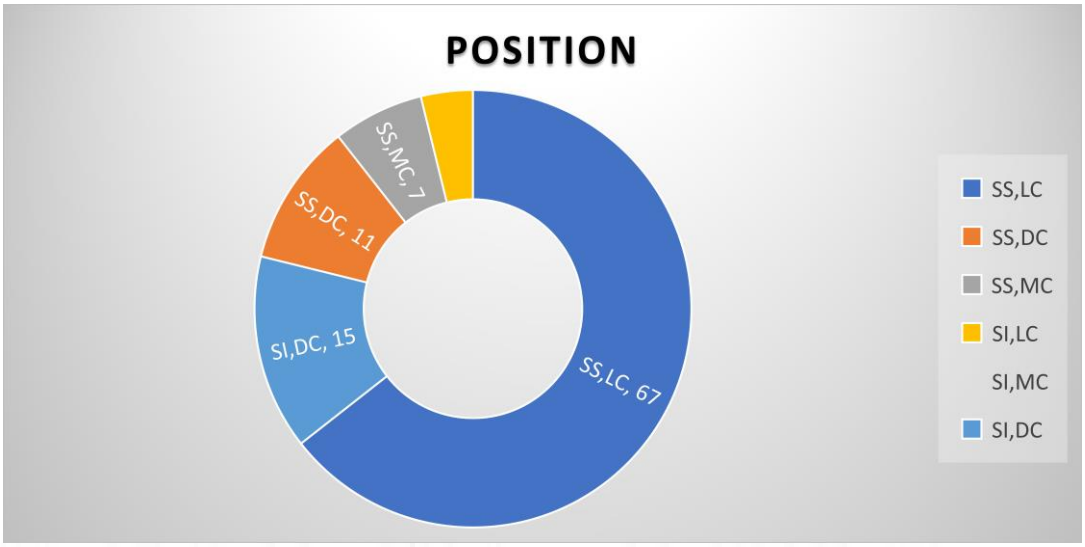


fig:14 showing distribution of position

Most of the study population was asymptomatic. The most common presenting symptom in the study population was dyspnoea (24%). Table-7 shows the various types of presentations.

Table-7

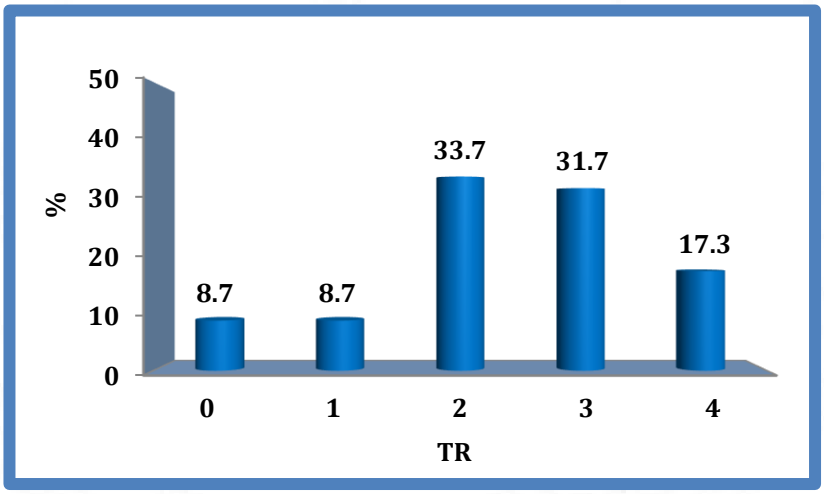
Presenting complaint	
Asymptomatic	38(36.5%)
Dyspnoea	25(24%)
Syncope	7(6.7%)
LRTI	15(14.4%)
Atypical Chest pain	5(4.8%)
Antenatally Detected	6(5.8%)
Palpitations	11(10.6%)

Nearly half of the patients had moderate or more than tricuspid regurgitation at presentation. Table-8 and figure-15 show the various grades of tricuspid regurgitation in the study population.

Table-8

TR	Frequency	%
0	9	8.7
1	9	8.7
2	35	33.7
3	33	31.7
4	18	17.3

figure-15

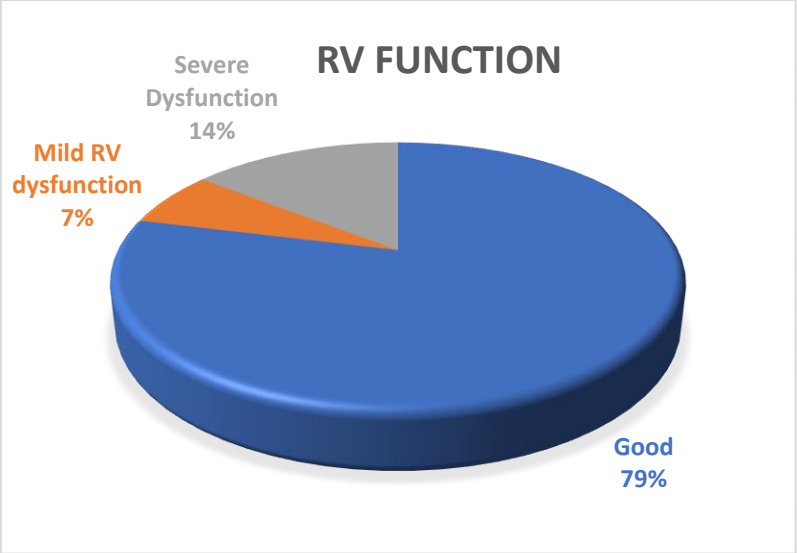


Most of the patients had good right ventricular (RV) function at presentation. RV dysfunction was seen in around 15 (14.4%). Table-9 and figure -16 show the RV function in the study population at presentation.

Table-9

RV Function	Frequency	%
Good	82	78.8
Mild RV dysfunction	7	6.7
Severe RV Dysfunction	15	14.4
Total	104	100.0

Figure -16

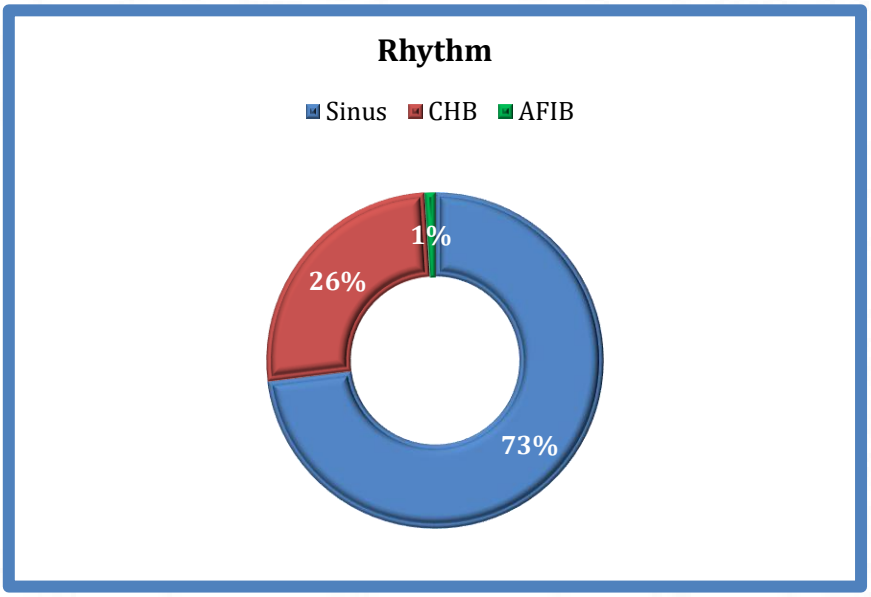


Around 27(26%) were noted to have complete heart block at their first visit. One patient was noted to have atrial fibrillation. Table-10 and figure-17 show the rhythm at the time of the presentation.

Table-10

Rhythm	Frequency	%
CHB	27	26.0
AFIB	1	1.0
Total	104	100.0

Figure -17

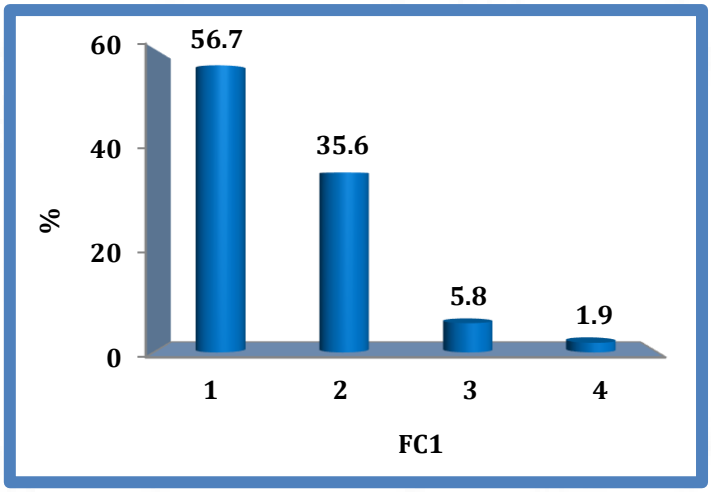


The majority of patients were in Functional Class (FC) I and around 8 patients were in FC III-IV. Table-11 and figure-18 show the distribution of the Functional class at presentation.

Table-11

FC1	Frequency	%
1	59	56.7
2	37	35.6
3	6	5.8
4	2	1.9
Total	104	100.0

Figure -18

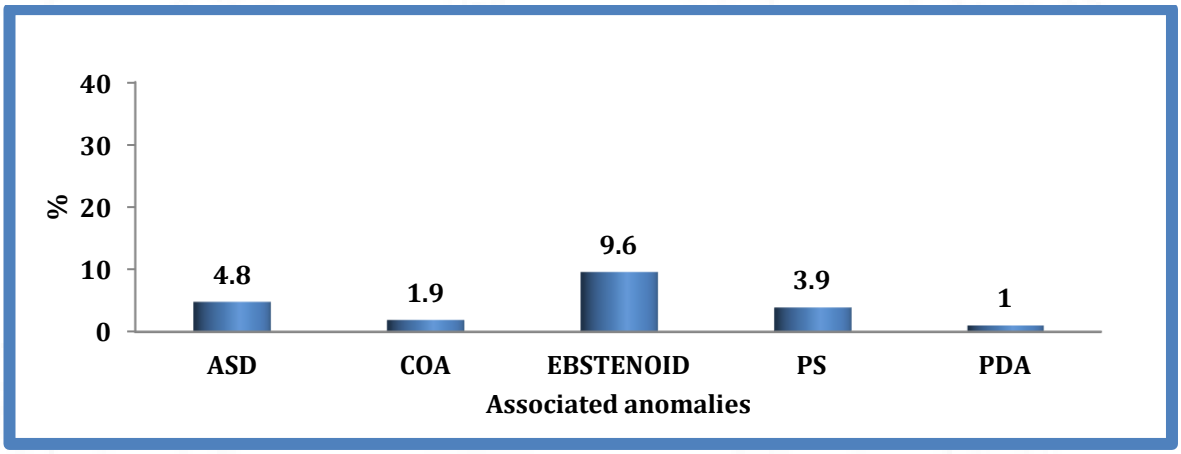


Some of the patients had associated anomalies such as Atrial Septal defects seen in 5 patients and Ebstenoid Malformation of the tricuspid valve was seen in 10 patients. Various other abnormalities are shown in table-12 and figure -19.

Table-12

Associated anomalies	Frequency	Percent
ASD	5	4.8
COA	2	1.9
EBSTENOID	10	9.6
PS	4	3.9
PDA	1	1.0

Figure -19



OUTCOMES

The patients were followed up for a median period of 5 years (2-14) (IQR). The median age at the last follow-up is 21.5 years (11-41).

On the last follow-up, tricuspid regurgitation improved in some and worsened in some patients. Some patients underwent PA banding and some patients underwent Tricuspid valve repair and Tricuspid valve replacement.

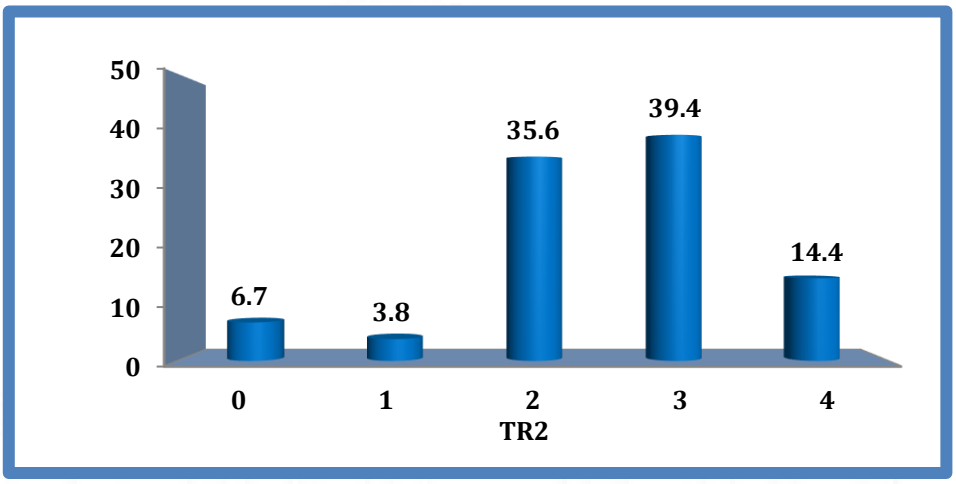
Table -13 and figure -20 show the tricuspid regurgitation on the last follow-up. Figure x shows the progression of TR from baseline to the last follow-up.

Table-13

TR2	Frequency	%
0	7	6.7
1	4	3.8
2	37	35.6
3	41	39.4
4	15	14.4
Total	104	100.0

More than moderate Tricuspid regurgitation was seen in around 56 patients on the last follow-up.

Figure -20-a



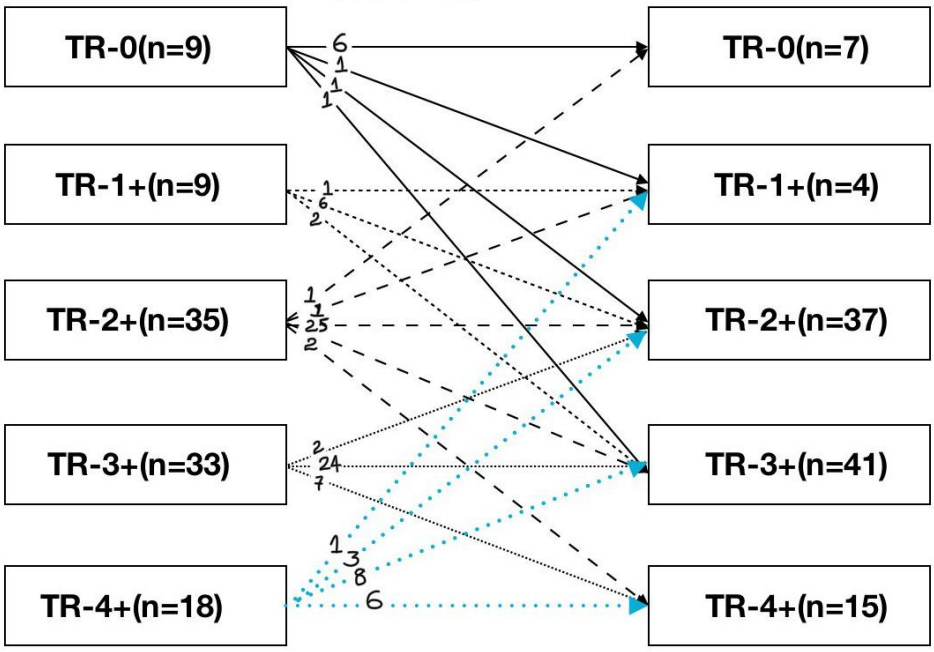


Figure -20-b shows the progression of TR from baseline to the last follow-up

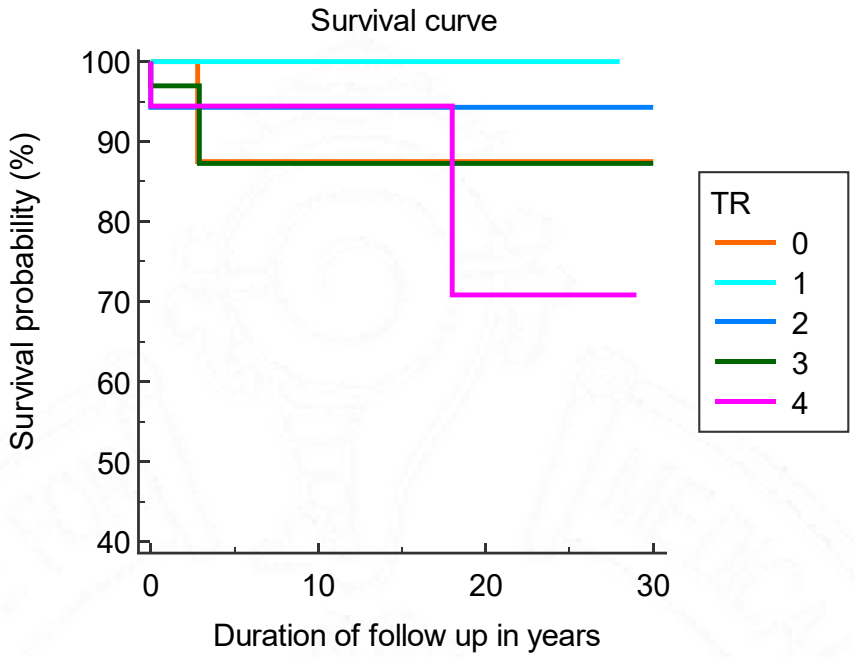


Fig:21- Kaplan Meier analysis showing survival probability with TR (p-0.864)

On follow-up, the right ventricular function was good in most of the patients. Some patients had deteriorated to mild RV dysfunction, while others developed Severe RV dysfunction. Table-14 and figure-22a show the RV function on the last follow-up. Figure x shows the progression of RV function from baseline to last follow-up.

Table-14

RV Function2	Frequency	%
Good	70	67.3
Mild RV dysfunction	16	15.3
Severe RV Dysfunction	21	20.2
Total	104	100.0

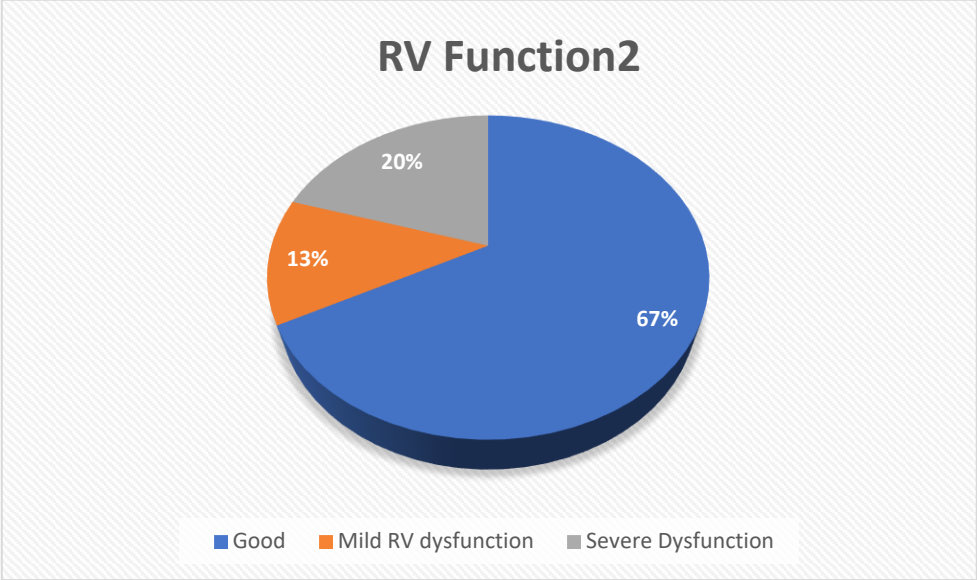


Fig:22-a shows RV function on follow-up

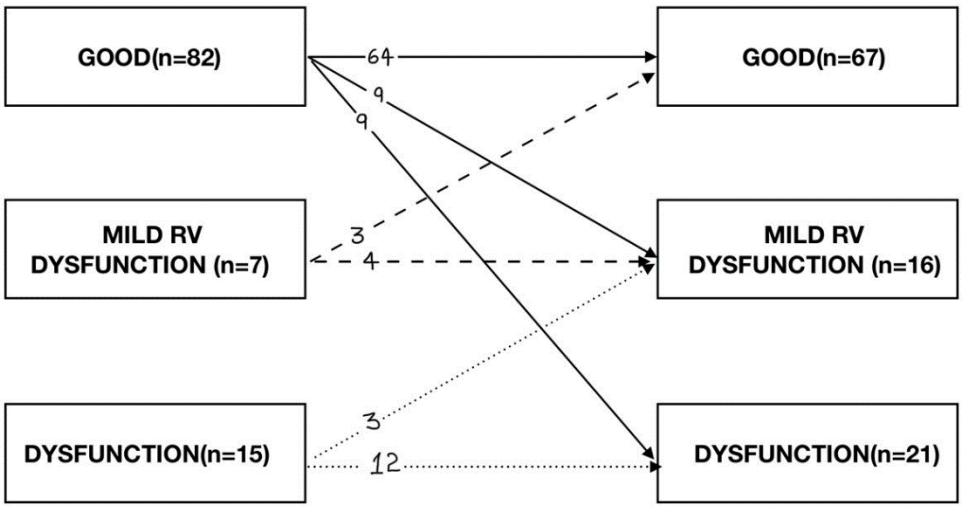


Fig:22-b comparison of RV function at baseline and in the last follow-up

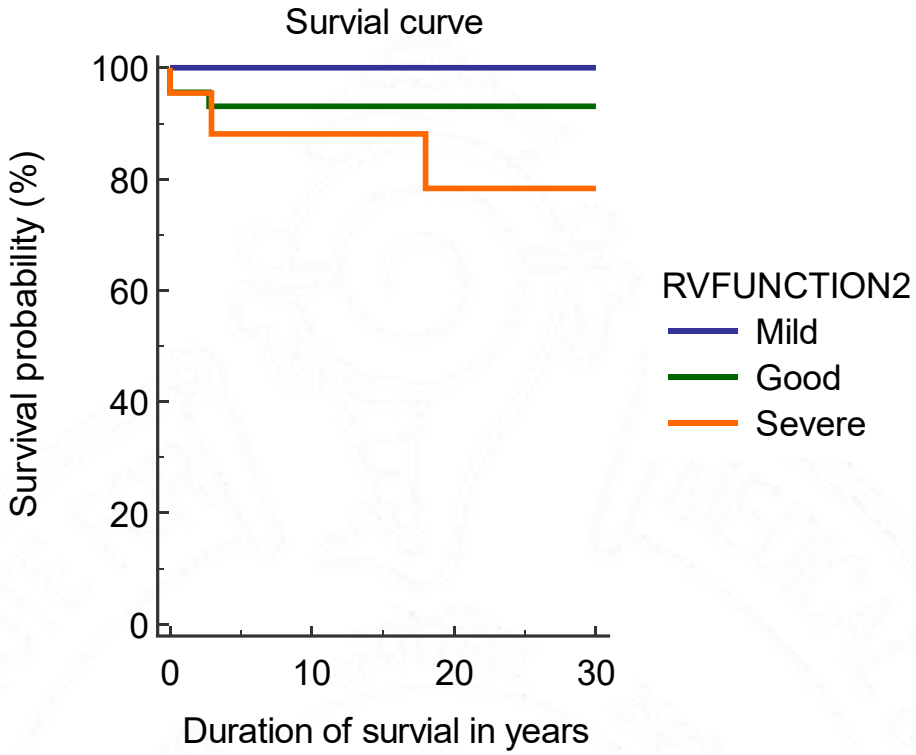


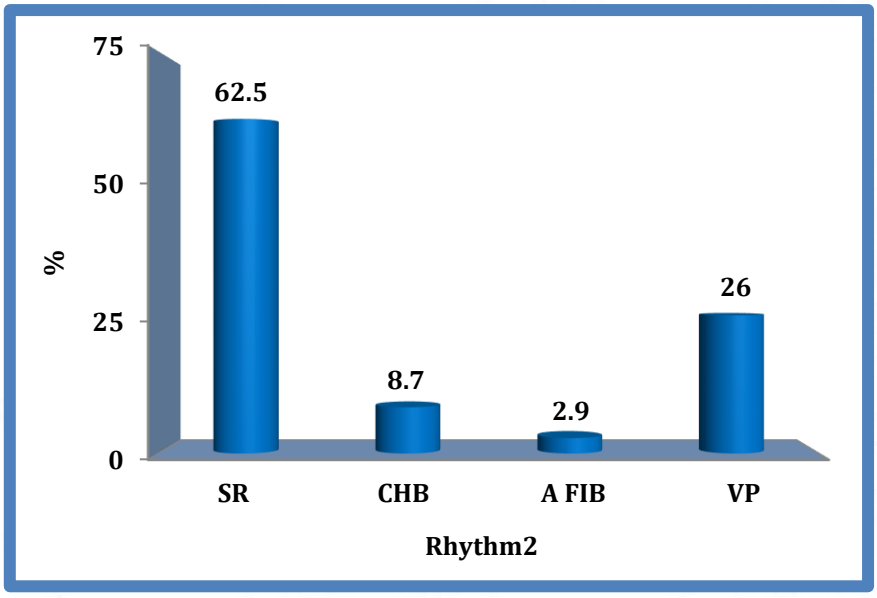
Fig:23-Kaplan Meier analysis shows the survival probability of RV function(p-0.047)

On follow-up, around 27 patients received Pacemakers, three patients were in atrial fibrillation, and nine patients had Complete Heart block. The mean age of development of CHB in our study is 27 years (2-73). The median age of patients who received pacemakers is 31 years (15-47.5) Table-12 and figure-24 show the rhythm of patients on the last follow-up.

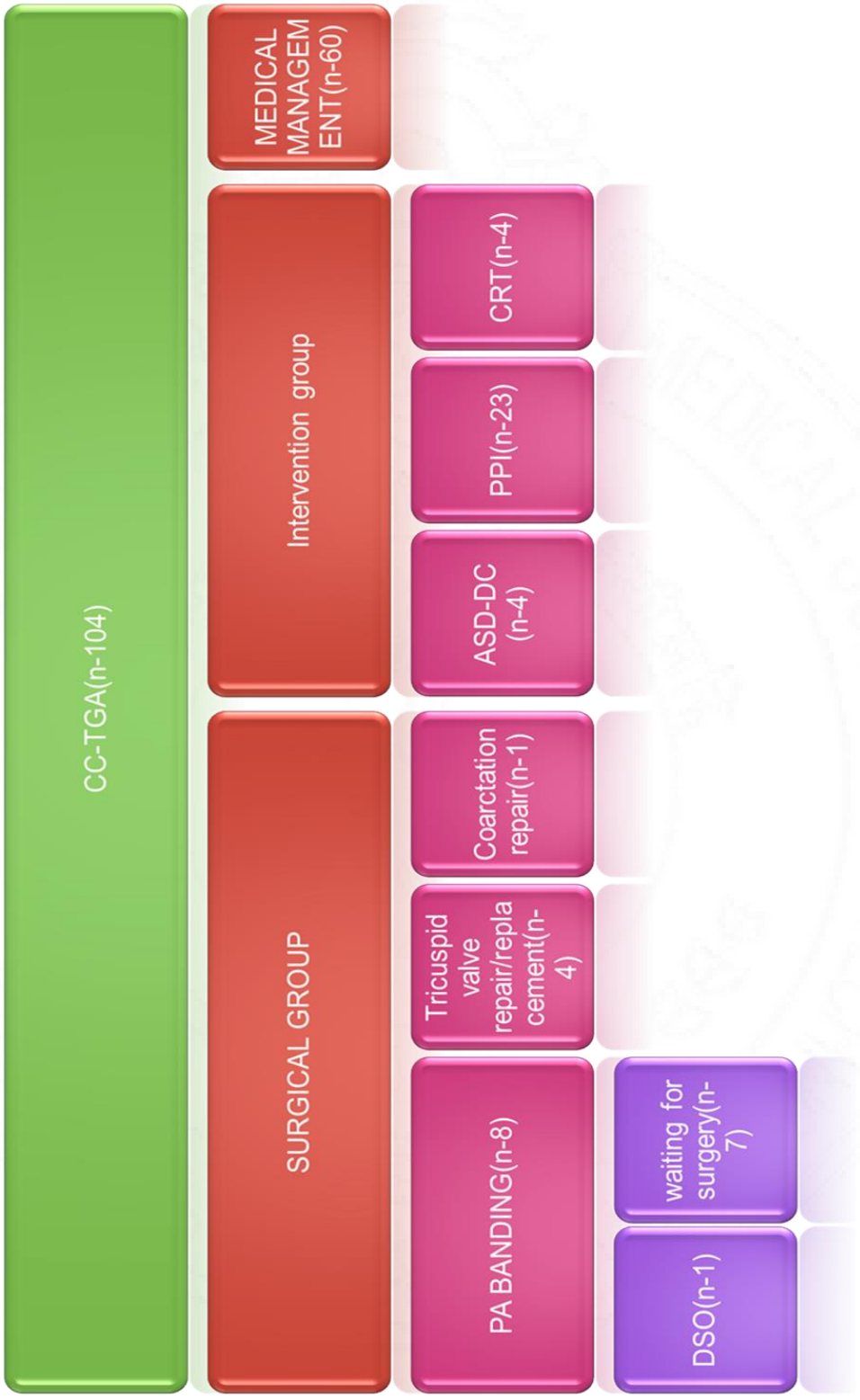
Table-15

Rhythm	Frequency	%
SR	65	62.5
CHB	9	8.7
A FIB	3	2.9
VP	27	26.0
Total	104	100.0

figure-24



SURGERY/INTERVENTIONS

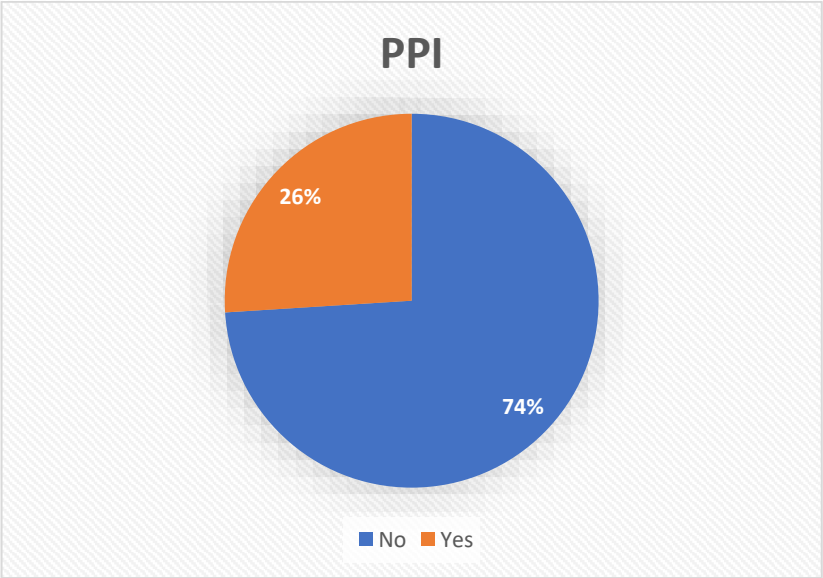


Around 27 patients received PPI in the population. Table -16 and figure-25 show the percentage of patients with CHB who received pacemakers. Four out of 27 received CRT.

Table-16

PPI	Frequency	%
No	9	25
Yes	27	75
Total	36	100.0

figure-25



Out of 27 patients, 8 patients had RV dysfunction at the time of implantation of PPI. On follow-up 13 patients had RV dysfunction. 5 new patients developed RV dysfunction. There was no association between PPI and the development of RV dysfunction(p-0.239).

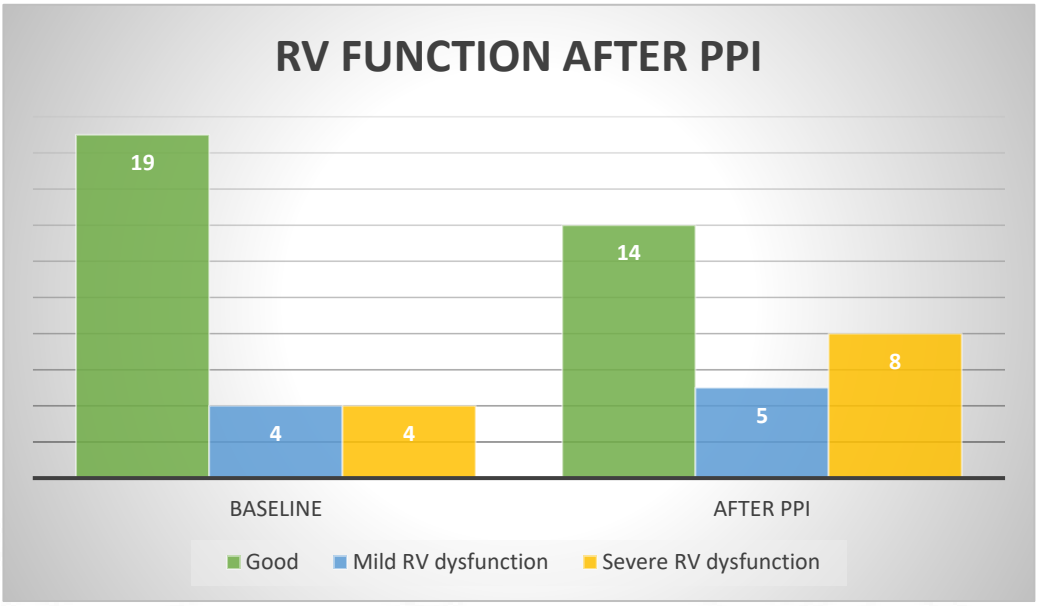


Fig:26-a RV function before and after PPI

Out of 27 patients, 15 patients had more than moderate TR at the time of implantation of PPI. On follow-up, 19 patients had more than moderate TR. There was no association between PPI and the development of TR (p-0.122).

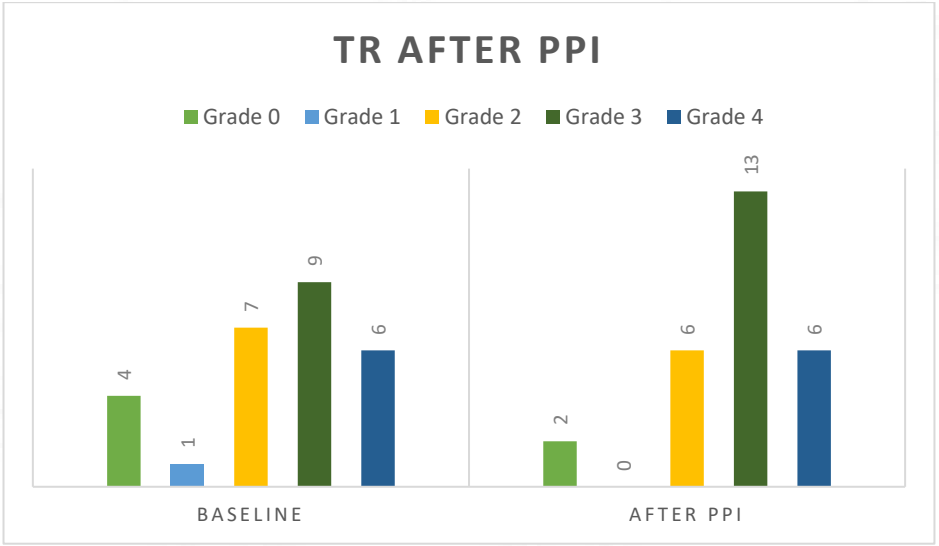


Fig:26-b TR before and after PPI

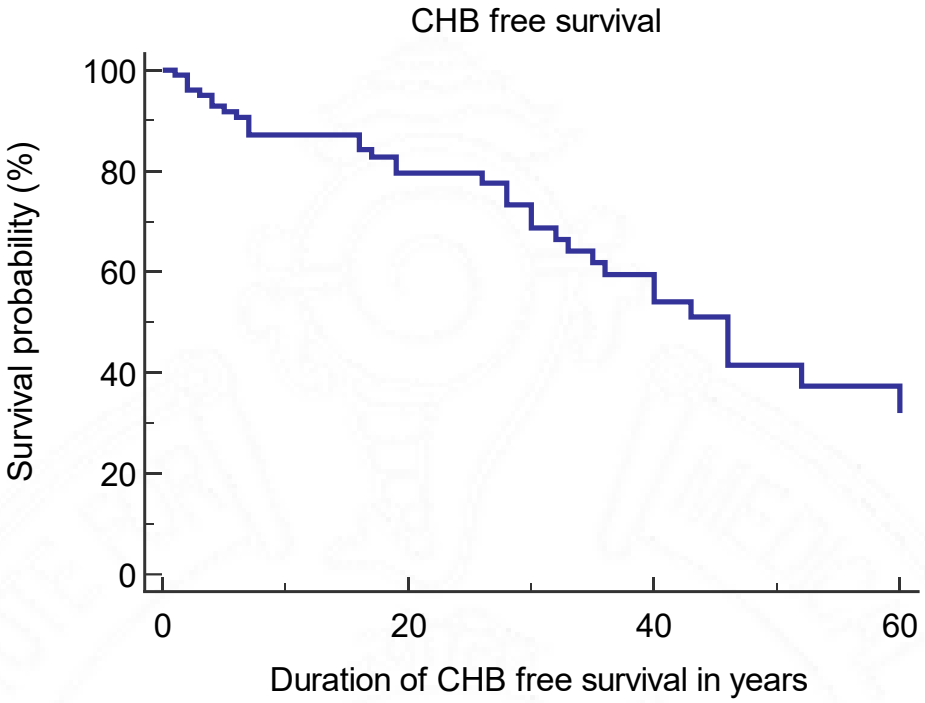
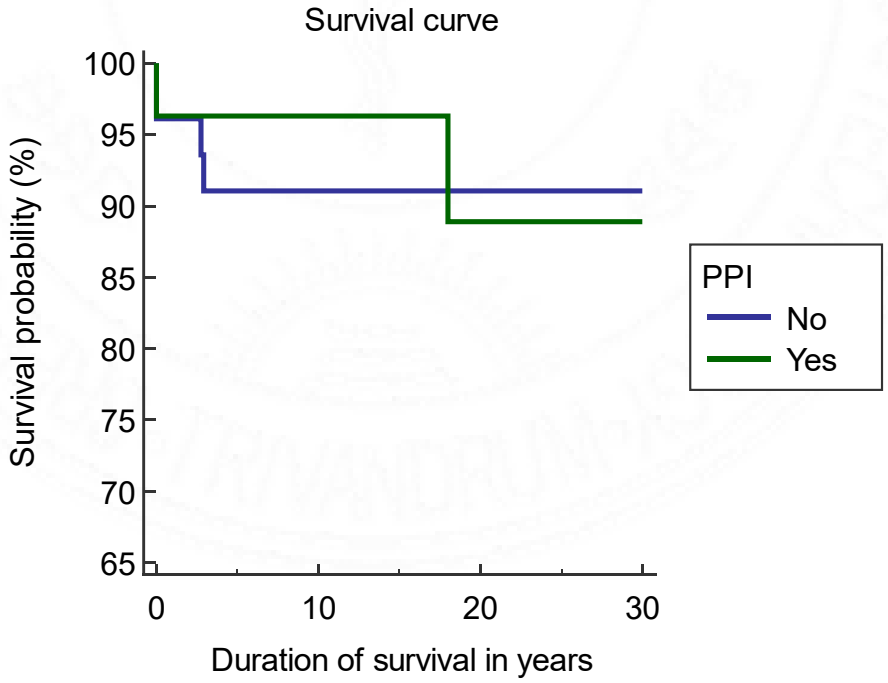


fig 27- Kaplan Maeir curves show the duration of CHB-free survival and the survival analysis in patients who received PPI. (p-0.440)



CRT was done in four patients. One patient underwent CRT at the age of 78 years and he expired on follow-up due to severe AVVR and dysfunction. The remaining three patients are on follow-up. There was no improvement in RV function but improvement in functional status is noted. Three patients underwent Right bundle optimised CRT under 3D electro-anatomic mapping.

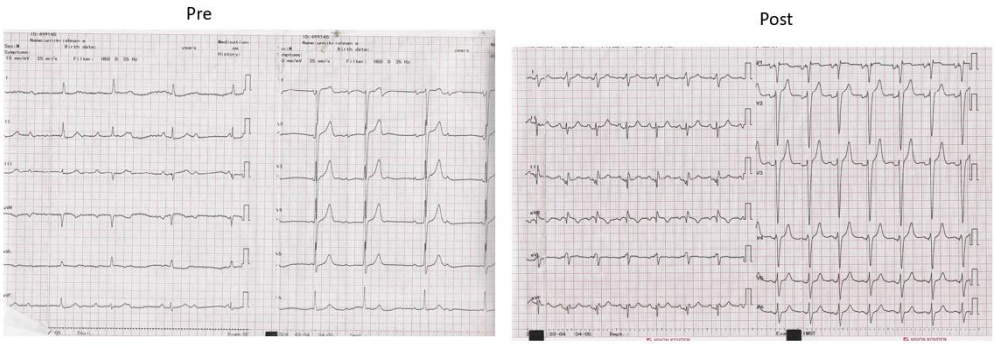


Fig:28-a ECG of a patient who underwent CRT

Fig:28-b Echo showing point of RBB capture

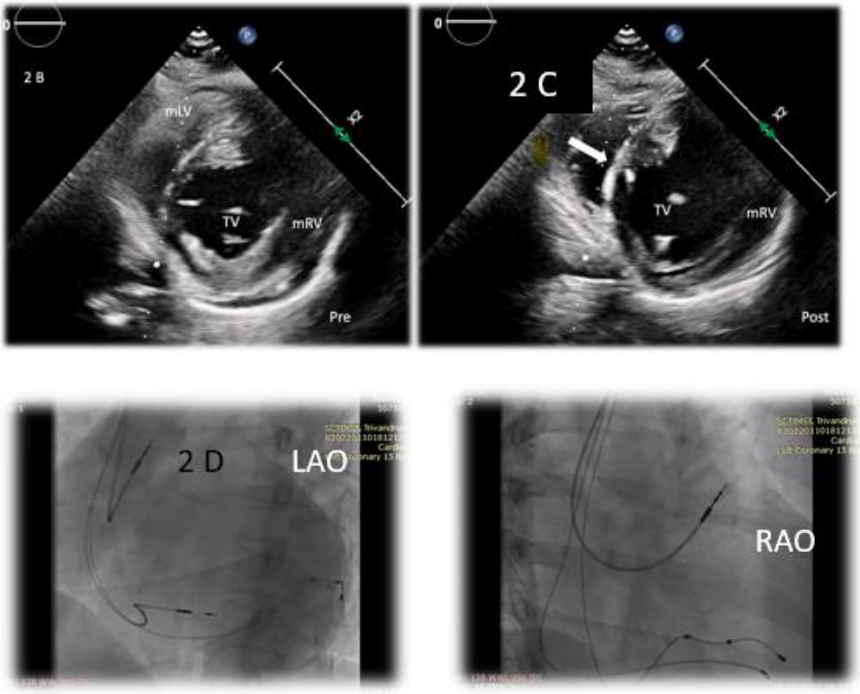


Fig:28-c Fluoroscopic image of CRT in LAO and RAO view

Around 8 patients underwent PA banding in our study population. The median age of pulmonary artery banding was 1.4 years (1-4). Out of 8 patients, one patient underwent Double Switch Operation. PA banding was done as destination therapy for TR in 1 patient and 5 patients are waiting for a double switch operation (DSO).

Table-17: Indication of PA banding in patients

	Age of PA banding	Indication	Follow up status
1	4 yrs	For AVVR	Severe TR
2	1 yr	AVVR+DSO	Severe TR
3	7 yr	AVVR	Mod TR+RV dysfunction
4	4 months	LV training	Mod TR
5	3 months	LV training	Sev TR
6	2 yrs	AVVR+LV training	Sev TR
7	1.4 yr	LV training	DSO
8	15 yr	AVVR+LV training	Mod TR

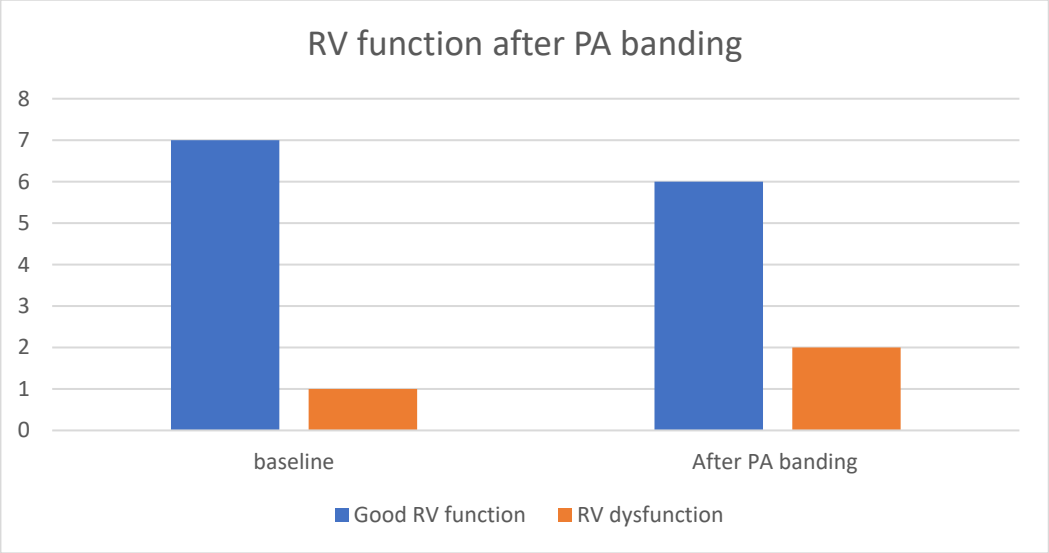


Fig:29-a Comparison of RV function at baseline and after PA banding (p-value-1.00)

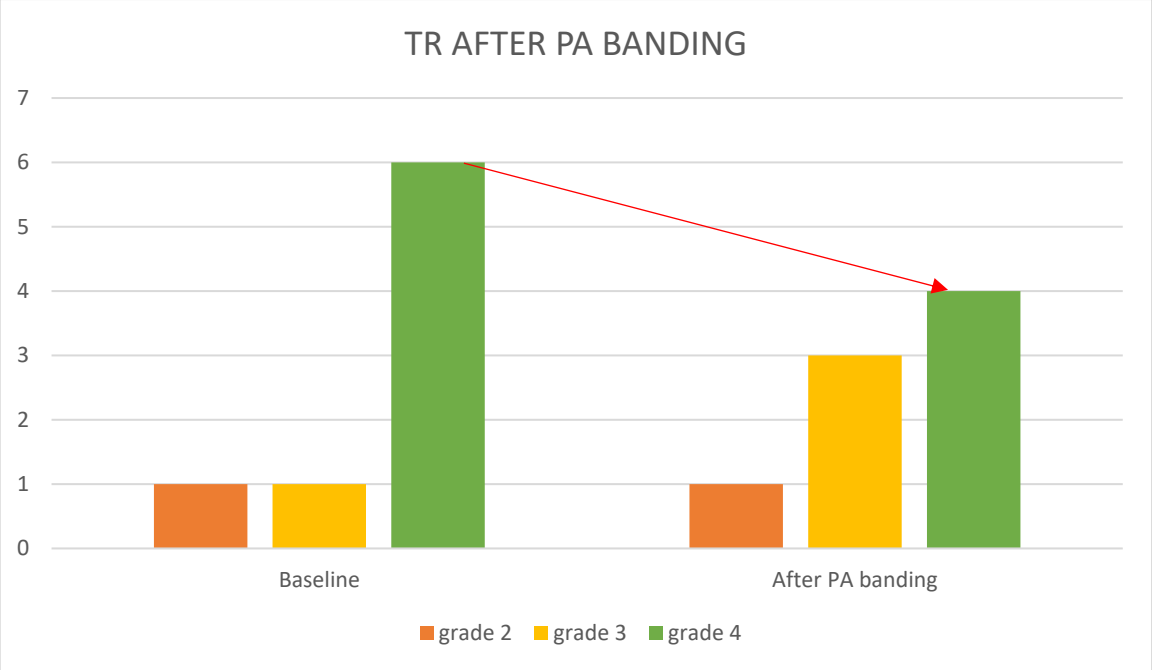


Fig:29-b Comparison of TR at baseline and after PA banding (p-value-0.043)

OTHER PROCEDURES:

Patients in the study population underwent various other procedures .EPS+RFA was done in eight patients which showed atrial tachycardia, AVNRT, accessory pathways, and prolonged intervals. One patient with Severe RV dysfunction had Polymorphic VT. An accessory pathway was seen in two patients. 3D electro-anatomic mapping was done in patients who underwent CRT.

Table-18: List of patients who underwent EPS

	n
Accessory pathway	2
AVNRT	2
Atrial Tachycardia	2
Polymorphic VT	1
EP study	1

One patient had coarctation of the Aorta which was repaired in the newborn period. 3 patients underwent Atrial septal defect Device closure. Two patients underwent Tricuspid valve repair, and two patients underwent Tricuspid valve replacement. Table-19 shows various procedures patients received.

Table-19

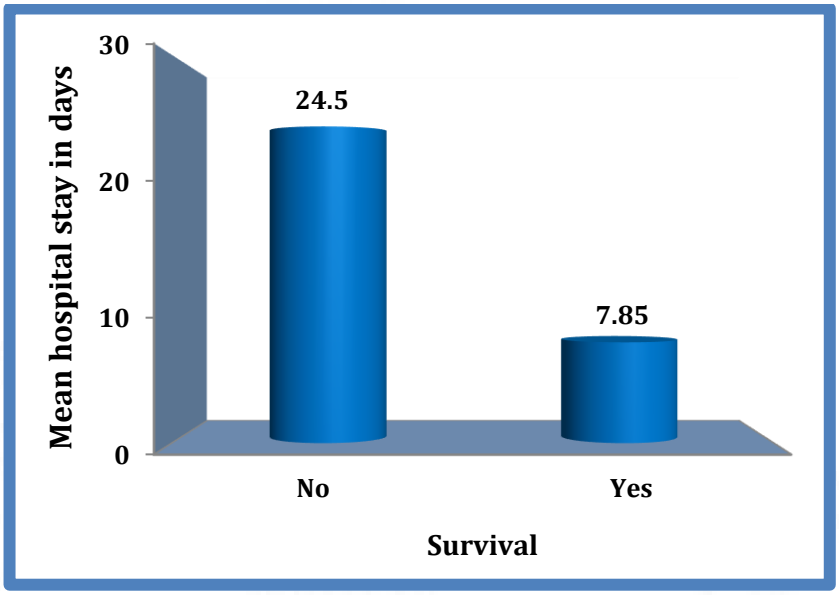
Procedure	n	Percent
ASD DC	3	2.9
CAG	4	3.9
COA Repair	1	1.0
CRT	4	3.9
EPS+RFA	8	7.7
PA Banding	8	7.7
PDA DC	3	2.9
PPI	23	22.11
Tricuspid Valve repair	2	2.0
TV Replacement	2	2.0

Hospital Stay and Mortality: Mean hospital stay in the mortality group was higher compared to the survival group. Duration of hospital stay is directly associated with mortality. ($p<0.002$). Table-20 and figure-30 show the mean hospital stay and mortality.

Table-20

Survival	Hospital Stay in days				P-value
	Mean	SD	Median	IQR	
No	24.50	9.40	25.50	18.00	**0.002**
Yes	7.85	7.47	4.50	7.25	

figure-30



Survival Analysis:

On follow-up,19 people could not be contacted and were removed from the survival analysis. Out of 85 remaining patients, 8 patients died. Six died due to Heart Failure due to systemic right ventricular failure. Table 21 and figure-31 show the survival of the population.

Table-21

Survival	Frequency	%
No	8	9.4
Yes	77	90.6
Total	85	100.0
Missing	19	
Total	104	

Figure -31

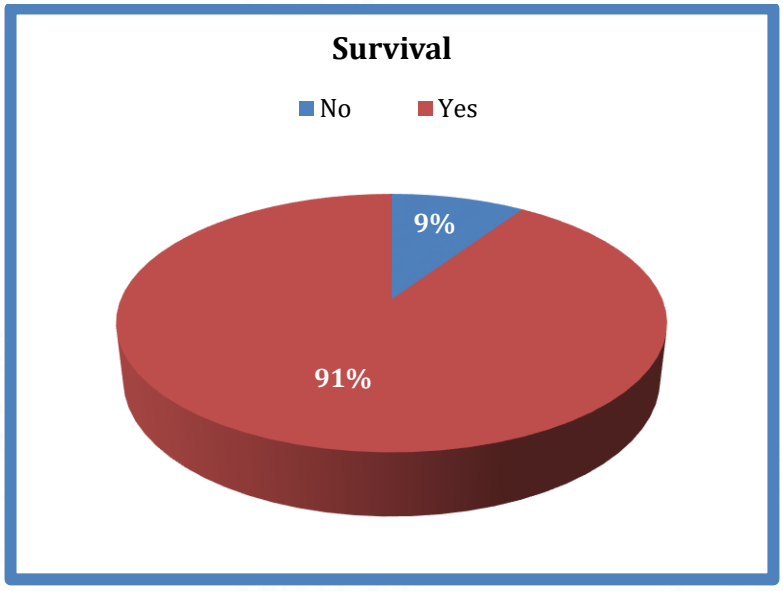


Table-22: Mortality in the study population

S.NO	RV FUNCTION	TR	AGE	SEX	EVENTS/COMMENT
1	Dysfunction	4+	22	M	Features of Heart failure
2	good	0	3	M	Sudden Death
3	Dysfunction	4+	81	M	Heart failure, CRT done
4	Dysfunction	2+	7	M	Underwent PA banding + TV repair, Heart failure
5	Dysfunction	3+	58	M	Heart failure
6	Dysfunction	2+	41	F	heart failure
7	good	2+	7	M	unknown
8	Dysfunction	4+	4	M	Heart failure

RV function on Follow-up is associated with mortality(p-0.047). TR ay baseline and follow-up and RV function had no influence on mortality. At 10 years of follow up around 95 % had freedom from mortality and which decreased to 92 % on follow up which is higher compared to the general population with normally structural heart.

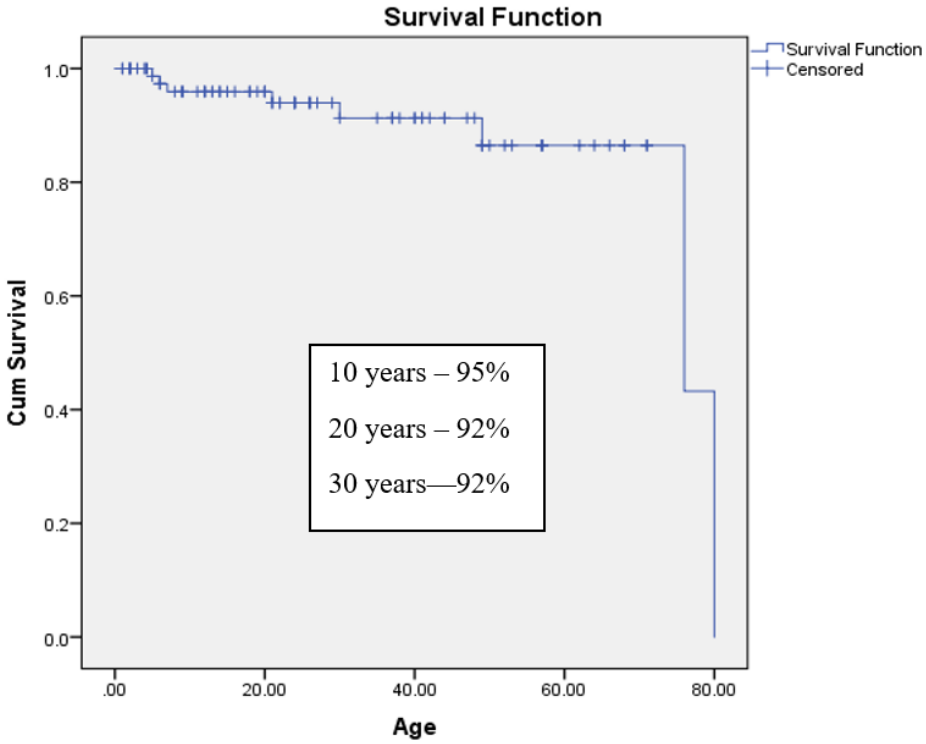


Fig 32: Freedom from mortality

Table-23: Univariate analysis for mortality

	Univariate analysis for mortality
TR at baseline	0.87
TR at last follow-up	0.78
RV function at baseline	0.74
RV function at last follow-up	0.047

6. DISCUSSION

Our study presents the long-term outcomes of patients diagnosed with CC-TGA with intact ventricular septum from a tertiary care centre in India. Most of the patients in the study population were kept on medical follow-up according to our institute policy. In 104 patients, around eight patients underwent PA banding. Only one patient underwent a Double switch operation (Hemi-Mustard +Arterial Switch Operation+ Right-sided Bidirectional Glenn and Left pulmonary angioplasty). This patient underwent PA banding before DSO. This patient received Pacemaker also.

Out of 104 patients,87 patients are kept on medical follow-up. Four patients underwent Tricuspid interventions, two had Tricuspid Valve repair, and two underwent Tricuspid Valve Replacement.

Multiple studies studied the natural history and outcomes of patients with a diagnosis of CC-TGA who are on medical management or underwent Anatomical repair or Physiological repair. Most previous studies included patients with associated defects such as Ventricular Septal Defect (VSD) and Pulmonary stenosis (PS). Our study excluded patients with Hypoplastic ventricles who underwent Univentricular Palliation and Ventricular Septal defect.

The physiology and outcomes of patients with associated anomalies differ significantly from those with Ventricular Septal defects to those with Intact Ventricular Septum. Patients with intact ventricular septum will have Left Ventricular Deconditioning early in infancy, in whom future Anatomical repair will be complicated without LV retraining. In patients with VSD and Pulmonic stenosis,

regression of LV takes time because of increased afterload. The timing of Anatomical repair in patients with intact ventricular septum is almost in the first decade of life, although the upper limit of timing is not routinely fixed.

Patients on medical management or who underwent Physiological repair are kept on follow-up based on earlier studies, which show that right ventricular function and Tricuspid valve can sustain systemic circulation in the long term(1,2). Our study supports the previous studies that patients with Right Ventricle as a systemic ventricle have excellent medium- and long-term outcomes. However, many patients had developed progressive Right Ventricular Dysfunction and Severe Tricuspid Regurgitation. In our study population, around 35% percent developed RV dysfunction on follow-up. The presence of right ventricular dysfunction on follow-up was associated with worse outcomes. Although it was expected, it helps in the stratification of patients with RV dysfunction and offers better medical management and management of complications earlier. The incidence of TR in our study is 55% which is high compared study by TP Graham et al. (40%)(T P Graham et al., 2000). Our study showed no positive correlation between the initial TR and RV function at presentation. Tricuspid regurgitation in CC-TGA is primarily due to progressive RV dysfunction and annular dilation, and most of the patients may have Ebstenoid malformation, but in our cohort, the incidence was 9.6 % which is much low compared to other studies.

In our cohort, one patient underwent DSO with Hemi mustard and ASO. This patient also received a Pacemaker. This patient was noted to have Severe LV dysfunction and RV dysfunction on follow-up. Dysfunction may be attributed to

pacing or late DSO. Previous data have suggested that older age at PAB and complete heart block are risk factors for systemic left ventricular dysfunction and mortality (Bautista-Hernandez et al., 2014; Myers et al., 2013b) Our patient received PA banding at the age of 1.4 years and received a pacemaker, which might contribute to his LV and RV dysfunction. Only one patient had undergone DSO in our cohort, so outcomes related to timing and repair cannot be analysed.

Typically, patients with CC-TGA may have an increased risk of developing Heart block because of two AV nodes and long nodal tracts. Usually, patients with an Intact ventricular septum don't require any ventricular surgery, whereas patients with VSD undergo patch closure or enlargement of VSD for LVOT. As the nodal tracts pass on the anterior border of the VSD, any surgery around the VSD may cause Heart Block. In our study population, around 27 patients had CHB at the first visit, and on the last follow-up, nine patients were noted to have Heart block. In a study by TP Graham incidence of CHB is around 27%. In a study by De León LE et al. incidence of CHB was approximately 20% with a median age of 9 months which is significantly less compared to our study(3). Around 14 patients received a Single chamber pacemaker, and 9 received a Dual chamber pacemaker. There was an increased incidence of RV dysfunction in patients with single-chamber pacemakers compared to Dual chamber pacemakers (Hofferberth et al., 2016).

Cardiac Resynchronisation Therapy may be a better option for patients requiring a Pacemaker as it prevents the development of ventricular dysfunction on follow-up(Moore et al., 2018). Development of heart block is important as it is associated risk of worsening RV and LV function(8). There was no influence of PPI on RV function on follow-up (P=0.14) in our study. There was no effect of PPI on

survival (P=1). In a study by Kharbanda et al., CRT for patients with systemic RV resulted in a marginal improvement in Ejection fraction and improvement in Functional status (Kharbanda et al., 2022). There were several case reports of successful CRT in ccTGA and improvement in functional status. In our study, around four patients received CRT. One patient expired on follow-up (The patient underwent CRT at the age of 78 years). The remaining three patients had improvement in functional status.

	Cui et al.		**TP Graham et al.**	**Our Study**
	No DSO n-90	**DSO n-37**	**n-50**	**n-104**
CHB	41%	43.2%	27%	36%
RV DYSFUNCTION	17.6%	8.1%	55%	37%
MORTALITY	4.7%	2.7%	-	7.69%
the median age of Pacemaker	23 years	4.5 years	23 years	31 years

Table-24: **Comparison with other studies**

In our study cohort, around eight patients underwent PA banding. Most of the patients will undergo DSO in the future. In the study by Cui et al. around 38%(n-49) underwent PA banding. PA banding was less in our institute because of our institute protocol of keeping asymptomatic patients on medical follow-up. In a study by Kai Ma et al., 40 patients underwent PA banding, out of which 15 patients underwent DSO, and the remaining patients were on medical follow-up. This study concluded that patients who had prolonged palliative pulmonary artery banding provided a lower mortality rate and indicated better cardiac function(10). In an Olivier Raisky et al.

study, 17 out of 44 patients underwent PA banding. This study concluded that Early PA banding helps in TR regression and adequate Left Ventricle training for Double Switch operation. In our study, one patient underwent DSO out of eight patients. One patient expired due to Severe RV dysfunction. The degree of Tricuspid regurgitation had come down after PA banding ($P < 0.043$), consistent with other studies. However, PA banding did not influence improvement in RV function($P=0.53$). There was no influence of PA banding on survival($P=0.53$).

Tricuspid regurgitation is an important determinant of RV function and vice-versa. More than half of the study population had more than moderate TR in our population. There was a direct correlation between RV dysfunction and the severity of tricuspid regurgitation ($p<0.001$). In our study, population 4 underwent Tricuspid valve interventions. Two patients underwent Tricuspid valve repair, and two underwent tricuspid valve replacement. The median age of tricuspid valve intervention is 18 years (10.8-26). In a Deng L et al. study, around 57 patients underwent TV interventions. Recurrent TR was frequently observed in patients who underwent Tricuspid valve repair and may be of limited utility in managing Tricuspid regurgitation(11). Recent advances such as Percutaneous Tricuspid valve intervention (Mitra clip) in patients of ccTGA with severe TR had good outcomes, but the timing of intervention and RV function determines the outcome (12). In a study by Liu R et al., out of 117 patients, 44 patients were IVS, and two patients underwent tricuspid valve interventions (13).

LIMITATIONS

- Single centre
- Retrospective study
- Advanced Imaging techniques can better assess RV Function
- Validation with Cardiac MRI for better hemodynamic assessment.
- Our institute follows medical management for CC TGA with IVS.

STRENGTHS OF THE STUDY

- It's a large cohort of ccTGA with intact ventricular septum from India
- Outcomes and incidence of RV dysfunction and tricuspid regurgitation were studied in the cohort.

7. SUMMARY

- The median age of diagnosis was 11 years (2.9-32.3).
- The cohort showed a majority male population.
- The most common position and Situs are Situs Solitus and Levocardia (n-64%), followed by Situs inversus and dextrocardia (n-14%).
- Around 36% are incidentally detected.
- About 40% of the patients had more than moderate tricuspid regurgitation, which increased to 54% on follow-up.
- About 20 % had RV dysfunction at baseline; on follow-up, incidence increased to 35%.
- The median follow-up period was five years (2-14).
- The incidence of Complete heart block was 34%, and three patients were noted to have Atrial fibrillation.
- Around 23 patients received PPI (14 had single chamber and 9 had double chamber pacemakers) and 4 patients received CRT.
- PA banding was done in 8 patients, and one underwent a Double switch operation.
- There was a decrease in TR regurgitation post-PA banding and no influence on RV function.
- Tricuspid regurgitation had a direct effect of worsening RV function and vice versa. If the tricuspid valve is structurally abnormal such as Ebstenoid it adds to the worsening of TR and RV dysfunction.

- Four patients underwent tricuspid valve interventions. (Two-tricuspid valve repair and two-tricuspid valve intervention)
- Mortality was seen in 8 patients, and 19 patients were lost to follow-up.
- Four patients underwent CRT, and there was an improvement in the functional status of the patients.

8. CONCLUSIONS

- The incidence of RV dysfunction was higher in patients with ccTGA with intact ventricular septum.
- More than half of the patients developed more than moderate Tricuspid regurgitation on follow-up.
- Earlier identification of Tricuspid regurgitation and intervention may prevent earlier development of RV dysfunction.
- The incidence of CHB was high due to the abnormality of conduction tissue in ccTGA.
- PA banding can be used as destination therapy for some patients with Moderate-Severe AVVR.
- In patients requiring pacemakers for CHB having ventricular dysfunction CRT could be a better option.

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ANNEXURES

Curriculum Vitae

Appendices

APPENDIX A – ETHICS COMMITTEE APPROVAL

APPENDIX D – PLAGIARISM CHECK REPORT

Curriculum Vitae

MALLA	PHANINDRA	
Last Name	First Name	Middle Name
Date of Birth (dd/mm/yy): 27/11/1992		Sex: Male
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator): Principal Investigator		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
Dr Malla Phanindra, Room No PG 306, Srishty hostel, Sree Chitra Staff Quarters, Kumarapuram, Thiruvananthapuram, 695011		Department of Cardiology SCTIMST
Mobile Number:9494694015		Email: mallaphanindra @gmail.com mallaphanindra@sctimst.ac.in

Academic Qualifications (Most recent qualification first)

Degree/Certificate	Year	Institution, Country
MD (General Medicine)	2020	Andhra Medical college, India
MBBS	2016	Rangaraya Medical College, India

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration] : Travancore Cochin council, **Reg no : 83710** , Dateof Registration: 09 Sep 2021

Current and previous positions (most recent position first)

Month and Year	Title	Institution/Company, Country
From JAN 2021 – till now	Senior Resident, Department of Cardiology	SCTIMST, India

Brief summary of relevant research experience:

1)MD THESIS-CLINICAL PROFILE AND OUTCOME OF DENGUE FEVER IN TERITIARY CARE HOSPITAL OF NORTH COASTAL ANDHRA

2)PAPER PUBLICATION-TO ASSESS THE FREQUENCY OF ETIOLOGICAL CAUSES OF PANCYTOPENIA IN NORTH COASTAL ANDHRA PRADESH

Current project/s at hand: NIL

Signature: 	Date: 23/11/2021 Place: Thiruvananthapuram

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

(IEC Regn No. ECR/189/Inst/KL/2013/RR-21)

SCT/IEC/1879/MAY/2022 06.09.2022

Dr. Malla Phanindra
Senior Resident
Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Malla Phanindra,

The Institutional Ethics Committee held on 13th May, 2022, reviewed and discussed your application to conduct the study titled "**LONG TERM OUTCOMES OF CONGENITALLY CORRECTED TRANSPOSITION OF GREAT ARTERIES (CC-TGA) IN A TERITIARY CARE CARDIAC CENTRE IN SOUTH INDIA**" (IEC/1879).

The following members of the Ethics Sub-committee were present at the meeting held on 13th May, 2022.

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
2.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
3.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
4.	Dr. P. Manickam	BSMS, MSc (Epid).,PhD	Male	Health Science Expert/ Social Scientist	No
5.	Adv. Priya Kaimal	LLM, MBL	Female	Legal Expert	No
6.	Dr. Manikandan.S	MBBS,MD,PDCC	Male	Clinician	Yes
7.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

The following documents were reviewed:

Original submission

1. Checklist Form
2. Reply to SRC comments
3. Covering letter addressed to the Chairperson, IEC, SCTIMST
4. Declaration form
5. IEC Application Form
6. Project Proposal
7. CV of PI and Co-PIs
8. Patient Information Sheet in English and Malayalam
9. Telephone Recruitment Script in English and Malayalam
10. Study Consent Form in English and Malayalam
11. Informed Consent (Assent Form) in English and Malayalam
12. Proforma
13. SRC Recommendation

Revised submission

1. Covering letter addressed to the Chairperson, IEC, SCTIMST dated 06.08.2022
2. Checklist Form
3. Covering letter addressed to the Chairperson, IEC, SCTIMST
4. Reply to SRC comments
5. Declaration form
6. IEC Application Form
7. Project Proposal
8. CV of PI and Co-PIs
9. Patient Information Sheet in English and Malayalam
10. Telephone Recruitment Script in English and Malayalam
11. Study Consent Form in English and Malayalam
12. Informed Consent (Assent Form) in English and Malayalam
13. Proforma

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,

Dr. G. Srinivas
Member Secretary, IEC

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST
THIRUVANANTHAPURAM

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST, THIRUVANANTHAPURAM

LONG-TERM OUTCOMES OF CONGENITALLY CORRECTED TRANSPOSITION OF GREAT ARTERIES WITH INTACT VENTRICULAR SEPTUM IN A TERTIARY

by Only 2 Genders

General metrics

55,182	8,341	1297	33 min 21 sec	1 hr 4 min
characters	words	sentences	reading time	speaking time

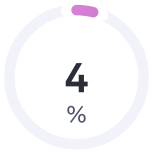
Score

This text scores better than 94% of all texts checked by Grammarly

Writing Issues

253	92	161
Issues left	Critical	Advanced

Plagiarism



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