CLINICAL OUTCOMES AFTER CARDIAC RESYNCHRONIZATION THERAPY: A SINGLE CENTER EXPERIENCE

Dr. SYED NAWAZ AFZAL

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SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, THIRUVANANTHAPURAM

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DECLARATION

I, **Dr. Syed Nawaz Afzal,** hereby declare that the project in this book titled "**CLINICAL OUTCOMES AFTER CARDIAC RESYNCHRONIZATION THERAPY: A SINGLE CENTER EXPERIENCE**" was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

Thiruvananthapuram
Date: 06/08/2021

Dr. Syed Nawaz Afzal
DM Trainee

CERTIFICATE

I, hereby certify that the work in this dissertation titled "**CLINICAL OUTCOMES AFTER CARDIAC RESYNCHRONIZATION THERAPY: A SINGLE CENTER EXPERIENCE**" is a certified record of original research work undertaken by Dr. Syed Nawaz Afzal done in the Department of Cardiology, in partial fulfilment of requirement for the purpose of award of D.M. cardiology degree.

Dr. Harikrishnan S, MD, DM
Professor and Head (Incharge),
Department of Cardiology
Sree Chitra Tirunal Institute for Medical Sciences and Technology
Thiruvananthapuram.

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Guide:

Dr. Narayanan Namboodiri K.K, MD,DM
Professor of Cardiology
Sree Chitra Tirunal Institute for Medical Sciences and Technology
Thiruvananthapuram- 695011

Co-Guides:

Dr Abhilash SP, MD, DM
Additional Professor of Cardiology
Sree Chitra Tirunal Institute for Medical Sciences and Technology
Thiruvananthapuram- 695011

Dr Krishna Kumar Mohanan Nair, MD,DM
Associate Professor of Cardiology
Sree Chitra Tirunal Institute for Medical Sciences and Technology
Thiruvananthapuram- 695011

TITLE

"CLINICAL OUTCOMES AFTER CARDIAC RESYNCHRONIZATION THERAPY: A SINGLE CENTER EXPERIENCE"

Primary Investigator:
Dr. Syed Nawaz Afzal, MD
Senior Resident
Department of Cardiology, SCTIMST.

Guide:
Dr. Narayanan Namboodiri K.K, MD,DM
Professor of Cardiology
Sree Chitra Tirunal Institute for Medical Sciences and Technology
Thiruvananthapuram- 695011

Co-Guides:
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Sree Chitra Tirunal Institute for Medical Sciences and Technology
Thiruvananthapuram- 695011

Dr Krishna Kumar Mohanan Nair, MD,DM
Associate Professor of Cardiology
Sree Chitra Tirunal Institute for Medical Sciences and Technology
Thiruvananthapuram- 695011

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Dr. Syed Nawaz Afzal

ABBREVIATIONS

2-D ECHO- 2 DIMENSIONAL ECHOCARDIOGRAPHY
ACC-AMERICAN COLLEGE OF CARDIOLOGY
ACE- ANGIOTENSIN CONVERTING ENZYME
ACS-ACUTE CORONARY SYNDROME
AHA- AMERICAN HEART ASSOCIATION
ARB-ANGIOTENSIN RECEPTOR BLOCKER
ARNI- ANGIOTENSIN RECEPTOR NEPRILYSIN INHIBITOR
BMI-BODY MASS INDEX
BSA-BODY SURFACE AREA,
CAD- CORONARY ARTERY DISEASE
CHF- CONGESTIVE HEART FAILURE
CRT-CARDIAC RESYNCHRONIZATION THERAPY
DCM: DILATED CARDIOMYOPATHY
DLP-DYSLIPIDEMIA
DM-DIABETES MELLITUS
ECG-ELECTROCARDIOGRAM
HCM-HYPERTROPHIC CARDIOMYOPATHY;
HF-HEART FAILURE
HR-HEART RATE,
HTN- SYSTEMIC HYPERTENSION
JVP-JUGULAR VENOUS PRESSURE
LA- LEFT ATRIUM
LBBB-LEFT BUNDLE BRANCH BLOCK
LGE- LATE GADOLINIUM ENHANCEMENT
LVEDD- LV END-DIATOLIC VOLUME
LVEF-LEFT VENTRICULAR EJECTION FRACTION
LVESV- LV END-SYSTOLIC VOLUME
LVH-LEFT VENTRICULAR HYPERTROPHY
LVIDD-LEFT VENTRICULAR END DIASTOLIC INTERNAL DIMENSION
LVIDS- LEFT VENTRICULAR END SYSTOLIC INTERNAL DIMENSION
LV-LEFT VENTRICLE
MI-MYOCARDIAL INFARCTION

MM-MIDMYOCARDIAL

MRA-MINERALOCORTICOID RECEPTOR ANTAGONIST,
MRI-MAGNETIC RESONANCE IMAGING

MR-MITRAL REGURGITATION

NYHA-NEW YORK HEART ASSOCIATION

PM-PACEMAKER

PND-PAROXYSMAL NOCTURNAL DYSPNEA

QRSD-QRS DURATION,

RBBB- RIGHT BUNDLE BRANCH BLOCK

RV- RIGHT VENTRICLE

RWMA: REGIONAL WALL MOTION ABNORMALITY

SEN-SUBENDOCARDIAL,

TM-TRANSMURAL,

SEM	:	STANDARD ERROR OF MEAN
ECG	:	ELECTROCARDIOGRAM
E.G.	:	FOR EXAMPLE
FIG	:	FIGURE
HR	:	HEART RATE
HR	:	HOUR
I.E.	:	THAT IS
MAP	:	MEAN ARTERIAL PRESSURE
MIN	:	MINUTE
MM HG:		MILLIMETERS OF MERCURY
NO	:	NUMBER
S	:	SECOND
SBP	:	SYSTOLIC BLOOD PRESSURE
SD	:	STANDARD DEVIATION
SPO2	:	SATURATION OF PERIPHERAL OXYGEN
VS	:	VERSUS

Introduction

Introduction

Heart failure (HF) is a significant health problem in South Asia. The estimated prevalence of HF in India ranges from 1.3 to 4.6 million, with an annual incidence ranging from 491,600 to 1.8 million.(1) Heart failure in India has postadmission mortality of 20%–30%. Medication adherence ranges from 25% to 50%, and the tolerance of guideline-based medication is low for Indian patients. Devices such as implantable cardioverter-defibrillators (ICD) and cardiac resynchronization therapy (CRT) devices, and left ventricular assist devices (LVAD) are available but not within reach of all. Patients with HF in India, compared with their western counterparts, have specific characteristics; they are younger, sicker, and have much higher morbidity and mortality.(2) Several studies demonstrated the safety and effectiveness of cardiac resynchronization therapy (CRT) combined with optimal drug therapy in the management of patients with moderate-to-severe HF.(3) Currently, CRT is a class I indication for patients with HF and LVEF <35%, LBBB and QRS duration of >150ms.(4)

Although cardiac pacing had been used historically to effectively treat bradycardia (delayed or absent activation of the entire ventricle), cardiac resynchronization therapy (CRT) introduced the concept of pacing to treat a delayed segment of the ventricle. When segments of the left ventricle (LV) contract with marked delay (most commonly of the free wall due to left bundle branch block [LBBB]), they fail to meaningfully contribute to stroke volume and cardiac output. This is termed dyssynchrony. Cardiac resynchronization improves ventricular function by pacing to improve electrical (and consequently mechanical) coordination and thus pump efficiency. It is accomplished by near-simultaneous pacing of the right ventricle (RV) and LV, most commonly using an epicardial lead in the coronary sinus to restore interventricular and intraventricular synchrony. This, in turn, improves LV contractility, stroke volume, and ejection fraction (EF).(5)

Dyssynchrony was first recognized in patients with cardiomyopathy and bundle branch block, who were noted to have a delay in the contraction of the posterior wall relative to the septum on M-mode echocardiography in 1994.(6) The presence of a left bundle branch block is associated with higher mortality in patients with heart failure.(7) CRT has been shown to reverse adverse cellular remodeling, improve ventricular function, lower levels of HF biomarkers (e.g., B-type natriuretic peptide), reduce HF hospitalization, and lower mortality.(8) However, CRT is not uniformly effective, and careful patient selection, lead positioning, and device programming are necessary to maximize its benefits.

A large proportion of CIED implants in India are pacemakers for bradyarrhythmias indications, predominantly AV block. Most CRT devices are implanted for NYHA Class III. There is a male predominance for implantation of CIED. (9) The benefits of CRT have been extensively studied in multiple randomized control trials; however, patients in those trials are meticulously selected, with stringent follow up, and hence may not reflect real-world data. Some studies done in India have shown clear superiority of CRT therapy over optimal pharmacological therapy in terms of improvement in clinical conditions among selected patients with HF.(10) Our study aims to add knowledge regarding the Indian scenario of CRT usage, it reflects the experience from a tertiary care center over a fairly long term follow up of patients with CRT.

Review of literature

The very essence of cardiovascular medicine is the recognition of early heart failure

Sir Thomas Lewis, 1933(11)

Cardiac pacing significantly improves the survival and quality of life in patients with bradycardia and/or dyssynchrony. When first introduced, pacemakers were simply lifesaving devices that provided a fixed pacing rate during bradycardia. With advances in technology and in our understanding of cardiac physiology, devices have been developed that can mimic normal cardiac automaticity and atrioventricular activation sequence and can approach the normal sequence of ventricular activation. These developments have led to a significant extension of the use of pacemakers so that now pacemakers are used to treat patients with bradycardia and a wide range of atrioventricular and intraventricular conduction disturbances. The latter relates to the condition of cardiac "dyssynchrony," for which cardiac resynchronization therapy (CRT) has been clinically introduced around the year 2000.

The use of CRT to treat patients with heart failure has given new impetus to a more comprehensive view on the role of intra-atrial, interatrial, interventricular, and intraventricular dyssynchrony, all factors that can be influenced in both a positive and negative way by cardiac pacing. It is now clear that a truly physiologic pacemaker maintains the normal sequence and timing of atrial and ventricular activation over a wide range of heart rates, can vary the heart rate in response to metabolic demands, and preserve the normal rapid, synchronous sequence of ventricular activation when required. (12)

Definition and classification of the problem (Heart Failure)

A universal definition of heart failure (HF) defines HF as the following: HF is a clinical syndrome with symptoms and or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and or objective evidence of pulmonary or systemic congestion. Revised stages of HF according to the consensus statement are as follows.

1. At-risk for HF (Stage A), for patients at risk for HF but without current or prior symptoms or signs of HF and without structural or biomarkers evidence of heart disease.
2. PreHF (stage B), for patients without current or prior symptoms or signs of HF, but evidence of structural heart disease or abnormal cardiac function, or elevated natriuretic peptide levels.
3. HF (Stage C), for patients with current or prior symptoms and/or signs of HF caused by a structural and/or functional cardiac abnormality.
4. Advanced HF (Stage D), for patients with severe symptoms and/or signs of HF at rest, recurrent hospitalizations despite guideline-directed management and therapy (GDMT), refractory or intolerant to GDMT, requiring advanced therapies such as consideration for transplant, mechanical circulatory support, or palliative care.(13)

The newly revised classification of HF based on LV ejection fraction includes

1. HF with reduced EF (HFrEF): HF with an LVEF of <40%;
2. HF with mildly reduced EF (HFmrEF): HF with an LVEF of 41% to 49%;
3. HF with preserved EF (HFpEF): HF with an LVEF of 50%; and

4. HF with improved EF (HFimpEF): HF with a baseline LVEF of <40%, a 10-point increase from baseline LVEF, and a second measurement of LVEF of >40%

Magnitude of problem in India

Heart failure (HF) is emerging as an important public health problem in India. With the dual burden of traditional diseases like rheumatic heart disease and the rising burden of new-age diseases like coronary artery disease, the burden of HF in India, is likely to be enormous. Also, the varying geographic and ethnic diversity poses a great challenge to the management of HF in our country.

Based on disease-specific estimates of prevalence and incidence rates of heart failure, a conservative estimate projects the prevalence of heart failure in India due to coronary heart disease, hypertension, obesity, diabetes, and rheumatic heart disease to range from 1.3 to 4.6 million, with an annual incidence of 491 600–1.8 million.(1)

The age at presentation with HF is dependent upon the level of epidemiological transition of that country. In the Trivandrum Heart Failure Registry (THFR) from India, the patients with HF were 10 years younger (mean age 61 years) compared to their western counterparts. In the INTER-CHF study, the mean age among Indians was 56 years, while the patients from sub-Saharan Africa were even younger, at 53 years. By contrast, the mean age at presentation was 72 years in the USA and the European data – the mean age was 70 years. The Kerala ACS registry also showed the presentation of ACS was at a younger age in India.(14)

Pathophysiology of dyssynchrony

When segments of the left ventricle (LV) contract with marked delay (most commonly of the free wall due to left bundle branch block [LBBB]), they fail to meaningfully contribute to stroke volume and cardiac output. This is termed dyssynchrony. Both RV pacing and LBBB

reduce systolic and diastolic function. These effects are independent of changes in preload and afterload.(15) This conclusion can be reached on the basis of results from studies using preparations in which preload and afterload were controlled, as well as those in which preload- and afterload-independent indices of ventricular function were determined.(16) The negative mechanical effect of dyssynchronous activation has been observed under various loading conditions, exercise, and in patients with and without coronary artery disease or impaired LV function.

As a consequence of the slower contraction and relaxation, isovolumic contraction and relaxation phases last longer, thus leaving less time for ventricular filling and ejection.(15)(16) Therefore it is not surprising that cardiac output and systolic arterial and LV pressures are also affected by dyssynchronous activation. In general, stroke volume is affected more than systolic LV pressure, presumably because baroreflex regulatory mechanisms partly compensate for the decrease in blood pressure. In addition to reduced stroke volume at unchanged preload, ejection fraction is usually found to be depressed during ventricular pacing as well as in LBBB. Similarly, ventricular pacing can increase pulmonary wedge pressure. The negative inotropic effect of ventricular pacing under various loading conditions is clearly illustrated by a rightward shift of the LV function curve, that is, the relationship between cardiac output and mean atrial pressure. (17) Later studies showed a rightward shift of the end-systolic pressure-volume (P-V) relation, thus suggesting that for each end-systolic pressure, the LV must operate at a larger LV volume.(17)

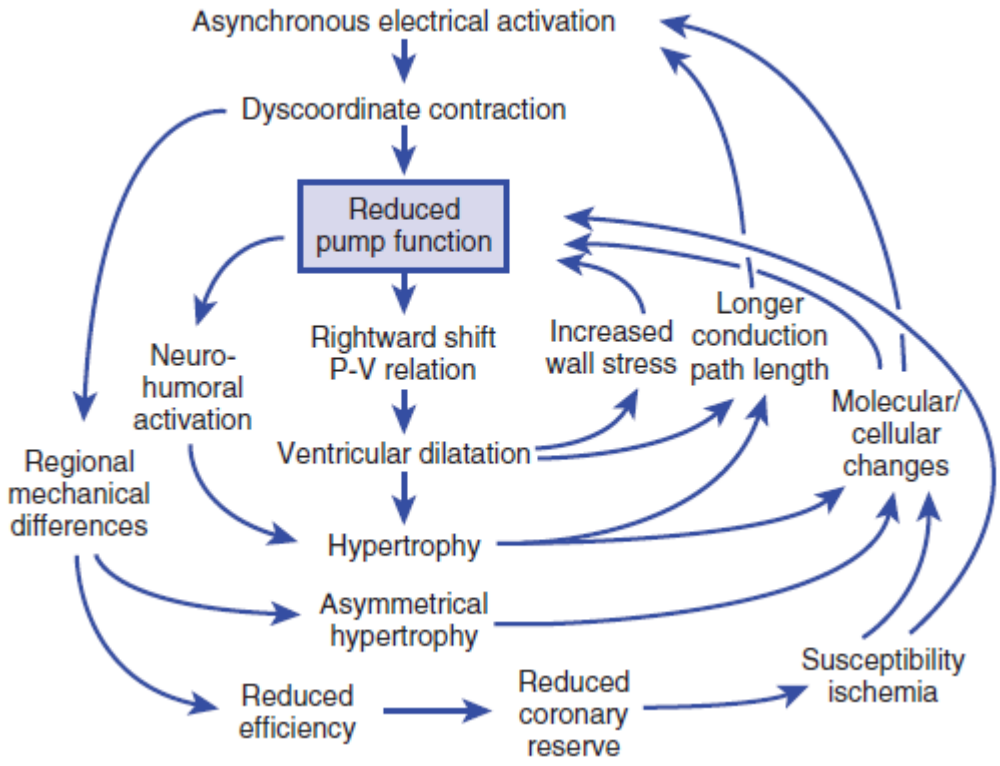

Figure 1: Possible relationships among the various consequences of dyssynchronous activation of the ventricles, due to ventricular pacing or conduction disturbances, and the deterioration of pump function over time. P-V, Pressure-volume.(12)

Mechanism of CRT in improving dyssynchrony

The essential novelty of CRT is that cardiac pacemakers no longer "just" maintained a normal heart rhythm but that they now also modify the sequence of atrial and ventricular conduction to improve pump function. Pacing at the LV lateral wall is used to create an activation wavefront, which moves in the opposite direction from a spontaneously occurring activation wavefront.(18) Consequently, during BiV pacing, two activation wavefronts are generated and merge approximately in the middle. A similar effect is obtained by single-site LV pacing using an AV interval that allows merging of the intrinsic activation originating from the RBB with the wavefront derived from the LV pacing lead. These merging wavefronts lead to less electrical dyssynchrony when compared with LBBB.(19)

CRT prolongs the time to maximum contraction and, by doing so, restores a more coordinated contraction pattern resulting in a more homogeneous distribution of regional loading conditions.(20) The improved cardiac pump function is expressed as higher LV dP/dT max, pulse pressure, cardiac output, and ejection fraction.(21) Improvement in pump function is also possibly mediated by reduction regurgitation of mitral and prolongation of diastolic filling time. These beneficial effects occur almost immediately after the start of resynchronization.(22) Such improved systolic pump function is achieved at unchanged or even lower filling pressures, denoting a true improvement of ventricular contractility through better coordination of contraction. Nelson and associates have shown that better coordination of contraction improves mechanical pump function while slightly decreasing myocardial energy consumption.(23)

The improved contractility and pump efficiency at a smaller end-diastolic volume reduce mechanical ventricular stretch. This latter reduction and the probably associated reduction in neurohumoral activation may well explain the beneficial reverse remodeling effect of CRT, such reverse remodeling points to a structural improvement in the myocardium.(22)

Landmark Trials in CRT

Multiple trials have shown clinical benefits after CRT implantation, they briefly summarized below:

Multisite Stimulation in Cardiomyopathy (MUSTIC) Trial: The MUSTIC trial, published in 2001, was the first large trial demonstrating the clinical benefits of CRT. It was a single-blind crossover study enlisting patients with New York Heart Association (NYHA) class III HF, LVEF ≤35%, left ventricle end-diastolic diameter >60 mm, and QRS duration >150 ms. The

MUSTIC investigators compared exercise tolerance and quality of life during active biventricular pacing for 3 months to exercise tolerance and quality of life during right ventricle–only backup pacing for a separate 3 months. The trial showed a statistically significant improvement in 6-minute walk distance (the primary endpoint), as well as improved quality of life and peak oxygen consumption following CRT. Because of the short duration of the study and crossover design, the study was not able to show a mortality difference. Nevertheless, the MUSIC trial was important because it was the first trial demonstrating clinical improvement with CRT and paved the way for later randomized controlled trials.(24)

Multicenter InSync Randomized Clinical Evaluation (MIRACLE) Trial: Reported in 2002, the MIRACLE trial randomized 453 patients in sinus rhythm with NYHA class III-IV HF, LVEF ≤35%, and QRS duration ≥130ms to receive biventricular pacing or no pacing. During the 6-month follow-up, CRT showed a decrease in hospitalizations because of HF as well as significant improvements in 6-minute walk distance, NYHA class, and quality of life score. A significant improvement in walking distance was noticed in the CRT group in as early as 3 months. In addition, the MIRACLE trial showed that resynchronization therapy is an effective adjunct to pharmacologic therapy in reducing the secondary combined endpoint of HF hospitalization or death. Despite these positive results, the MIRACLE trial was not sufficiently powered to detect an improvement in mortality with CRT.(25)

Comparison of Medical Therapy, Pacing, and Defibrillation in HF (COMPANION) Trial: The COMPANION trial included 1,520 patients and was the first trial able to detect improvement in the primary combined endpoint of hospitalization or death from any cause. The trial enrolled patients with NYHA class III-IV HF, LVEF ≤35%, and QRS duration >120ms. The trial had 3 treatment arms: patients were randomly assigned to optimal medical therapy (OMT) alone,

OMT plus CRT with pacing only (CRT-P), or OMT plus CRT with a defibrillator (CRT-D). At one year, the CRT-D group, but not the CRT-P group, had a

significant reduction in overall mortality compared to the group receiving OMT alone. The CRT-P group barely missed statistical significance for overall mortality (p=0.059). The exciting results of the COMPANION study showed that CRT-D had a definite mortality benefit and suggested that CRT may improve mortality, even in the absence of a defibrillator.(8)

Cardiac Resynchronization-HF (CARE-HF) Trial: In 2005, the CARE-HF trial attempted to clarify the mortality benefit of CRT independent of the mortality benefit of defibrillation. This trial enrolled 813patients with NYHA class III-IV HF, QRS duration ≥120 ms, echocardiographic dyssynchrony, and LVEF ≤35%. Of note, the vast majority of CARE-HF subjects had a very long QRS duration (median 160ms). Only approximately 8% of patients had QRS duration between 120-150ms, and enrolment of these patients required mechanical dyssynchrony as determined by echocardiography. The primary endpoint was a composite of all-cause mortality or hospitalization for a major cardiovascular event, and the secondary endpoint was all-cause mortality. Compared to OMT alone, CRT-P was associated with a significant (26%) reduction in all-cause mortality and hospitalization for major cardiovascular events at 29 months. Most important, CARE-HF was the first trial to show definitively that CRT-P had a mortality benefit, even in the absence of implantable cardioverter-defibrillator (ICD) therapy.(3)

Multicenter Automatic Defibrillator Implantation with Cardiac Resynchronization Therapy (MADIT-CRT) Trial: In 2009, the MADIT-CRT trial randomized 1,820 patients with LVEF ≤ 30% and QRS duration ≥150 ms to biventricular pacing or no-pacing groups. Significantly, the MADIT-CRT trial enrolled patients with mild (NYHA class I-II) HF, a group that had previously been excluded from CRT trials. This study showed that CRT produced a 29% reduction in the primary combined endpoint of HF events (defined by a need for intravenous diuretics) and mortality. However, further analysis showed that this reduction was derived almost exclusively from HF events, slightly weakening the impact of the study. Nonetheless, MADIT-CRT demonstrated that even mildly symptomatic HF patients might benefit from CRT.(26)

Resynchronization-Defibrillation for Ambulatory HF (RAFT) Trial: The RAFT trial helped delineate the mortality advantage conferred by CRT independent of defibrillation. The trial randomized 1,798 patients with NYHA class II-III HF, LVEF ≤30%, and QRS duration ≥120ms to receive either an ICD alone or an ICD plus CRT. The study recorded that CRT produced a 7% reduction in the primary outcome of death from any cause or hospitalization for HF. RAFT further confirmed the benefits of CRT over and above the benefits of defibrillator therapy alone.(27)

Randomized Trial of Cardiac Resynchronization in mildly symptomatic Heart Failure patients and in asymptomatic patients with Left Ventricular Dysfunction and previous Heart Failure symptoms(REVERSE trial): The REVERSE Trial, published in 2008, studied the effects of cardiac resynchronization therapy (CRT) in New York Heart Association(NYHA) functional class II heart failure (HF) and NYHA functional class I (American College of Cardiology/American Heart Association stage C) patients with previous HF symptom. Six

hundred ten patients with NYHA functional class I or II heart failure with a QRS ≥120 ms and a LV ejection fraction ≤40% received a CRT device (±defibrillator) and were randomly assigned to active CRT (CRT-ON; n =419) or control (CRT-OFF; n = 191) for 12 months. The primary endpoint was the HF clinical composite response, which scores patients as improved, unchanged, or worsened. The prospectively powered secondary endpoint was LV end-systolic volume index. Hospitalization for worsening HF was evaluated in a prospective secondary analysis of health care use. The HF clinical composite response endpoint, which compared only the percent worsened, indicated 16% worsened in CRT-ON compared with 21% in CRT-OFF (p = 0.10). Patients assigned to CRT-ON experienced a greater improvement in LV end-systolic volume index (-18.4 ± 29.5 ml/m2 vs. -1.3 ± 23.4 ml/m2, p <0.0001) and other measures of LV remodeling. Time-to-first HF hospitalization was significantly delayed in CRT-ON (hazard ratio: 0.47, p =0.03). The REVERSE trial demonstrated that CRT, in combination with optimal medical therapy (±defibrillator), reduces the risk for heart failure hospitalization and improves ventricular structure and function in NYHA functional class II and NYHA functional class I (American College of Cardiology/American Heart Association stage C) patients with previous HF symptoms.(28)

Hypothesis, Aims and Objectives

Hypothesis:

- The clinical response to CRT is modified by many associated factors.
- The response rate to CRT on follow-up in a well-monitored device clinic is comparable to the Western data.

Aims and Objectives:

1. To assess clinical outcomes in patients who underwent CRT P/D implantation
2. To elucidate factors that determine response to CRT as in improvement in NYHA class, ECG (QRS duration) and Echocardiographic (LVEF, Endsystolic volumes) parameters

Materials and Methods

In this hospital-based study, patients who have undergone CRT implantation from January 2004 to December 2019 were taken up for analysis

252 patients who underwent CRT implantation as per international guidelines in our institution from January 2004 to December 2019, fulfilling the eligibility criteria, were enrolled in this study. This study was approved by the institutional ethical committee.

- **Study Design:** Retrospective, observational study
- **Subject selection:**

  Inclusion criteria

  - All consecutive patients who had undergone CRT P/D implantation from January 2004 till December 2019.

  Exclusion criteria

  - Those who had implants in other centers but being followed up in our device clinic
- Characteristics at baseline and data of all follow-up visits are collected from EMR.
- The last follow-up data were acquired in June 2021
- **Place of study**: Department of Cardiology, SCTIMST
- **Sample size** – 252 patients

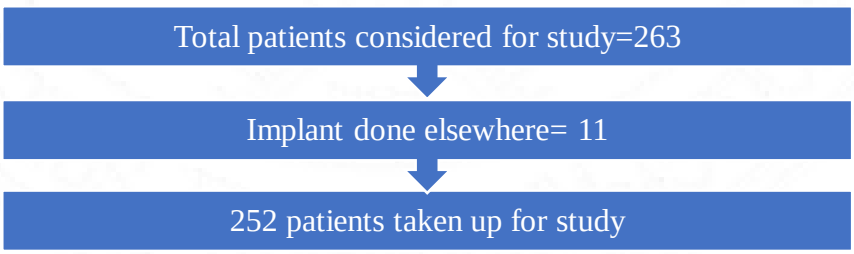

Figure 2: Study Flow Chart

Study factors:

1. **Hypertension:** Hypertension was defined as a blood pressure of higher than 140mm Hg systolic and/or 90mm Hg diastolic (mean of three measurements for cases) or use medications for hypertension.
2. **Coronary Artery Disease:** Signs, Symptoms, ECG changes, Exercise test (TMT), Coronary angiography suggestive coronary artery disease or ischemic heart disease.
3. **Diabetes mellitus:** According to ADA definition of diabetes, A1C of greater than or equal to 6.5%, or fasting blood glucose of greater than or equal to 126 mg/dl, or random blood glucose of greater than or equal to 200 mg/dl.
4. **Atrial Fibrillation**: Signs, Symptoms and ECG changes of Atrial fibrillation.
5. **Uncontrolled Hypertension**- Systolic blood pressure of more than 180 mm of Hg and Diastolic blood pressure of more than 110 mm of Hg.
6. **Systolic Dysfunction**: Ejection fraction of less than 50% assessed by 2D-Echocardiography. Ejection fraction was calculated by Fractional shortening; Fractional Shortening= [(LVEDD-LVESD)/LVEDD] x 100
7. **Dyslipidemia**: Defined by ATP III guidelines.
8. **Smoking**: Defined by the history of addiction to tobacco smoking as per history was given by patient or relatives.
9. **Heart failure:** Defined by physical signs and symptoms of heart failure according to ESC criteria.
10. **Responders vs Non-responders:**

    Response to CRT: change in LVEF >/= to 5% with improvement in NYHA functional class by at least one

    Non-responders- Change in LVEF < 5% with worsening NVHA functional class or no improvement in NYHA functional class

11. **New York Heart Association Classification:** Using a categorical system, the patient's ability to perform different levels of physical activity is graded. The symptoms have previously been shown to correlate with the degree of LVSD and prognosis. The grading system is described below:

    NYHA I: No limitation in physical activity.

    NYHA II: Slight limitation in physical activity

    NYHA III: Marked limitation in physical activity

    NYHA IV: Unable to carry out physical activity without discomfort. Symptoms at rest

12. **Non-ischemic cardiomyopathy**: defined as normal coronary and LVEF<35%
13. **Ischemic cardiomyopathy**: defined as LVEF <35% and significant coronary involvement
14. **Cardiac cause of death**: defined as death due to Congestive cardiac failure, VT storm, Myocardial infarction, Sudden cardiac death.

Observations:

The observations will be noted by the principal investigator, and confidentiality will be maintained regarding patient identification. Data will be stored by the principal investigator on his personal computer for three years.

Patient's name:

Age: Years Sex: M/F H. No:

Home Town: Contact No:

Diagnosis:

CLINICAL FEATURES

- NYHA CLASS

Past Medical History:

- CV Risk Factors : DM / HT / Smoking / PVOD / Prior CHF/AF

ECG Findings:

- Heart Rate :
- Rhythm :
- QRS Duration:

Echo Findings:

- LVEF
- LV DD- S- D-
- IVS- S- D-
- PW- S- D-
- ESV, EDV
- SPWD, Interventricular delay
- Mitral Regurgitation: Absent, Trivial, Mild, Moderate, Severe
- RV dysfunction : Yes / No

MRI Findings:

- LVEDD
- LEEDS
- LVEF
- Gadolinium enhancement
    - Epicardial:
    - Mid-Myocardial:
    - Sub-endocardial:
    - Transmural

Lead position:

QLD time:

Device parameters:

TREATMENT RECEIVED:

- DIURETICS
- LOOP DIURETICS
- POTASSIUM-SPARING DIURETICS
- OTHERS
- BETA-BLOCKERS
- ACE INHIBITORS

- ARB

Statistical Analysis

- Continuous data were expressed as mean±SD
- Categorical data were presented as numbers and percentages.
- Independent-sample t-test for continuous variables and Chi-square test for categorical variables.
- Multivariate analysis was used to find significant predictors of outcome
- Kaplan Meier analysis was used to find survival patterns
- p-value of <0.05 was considered significant

Observations and Results

A total of 252 patients fulfilling the inclusion criteria who underwent CRT implantation between January 2004 and December 2019 were recruited in the study. Mean Follow up period being 4.5 ±2.6 years.

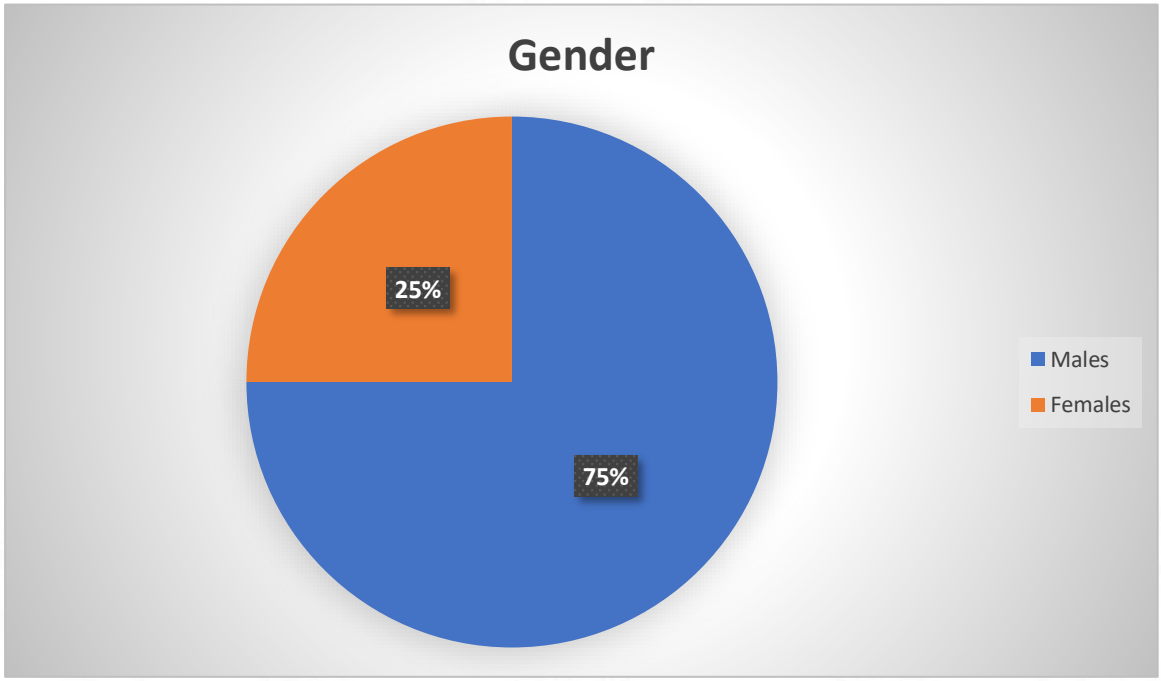

Figure 3: Gender distribution in the study population

Of the total patients recruited, males (n=189) outnumbered females (n=63) ; ratio of 3:1. The following are the results and observations.

Table 1: Baseline Demographic features

VARIABLE	MALES (n=189) (SD)	FEMALES (n=63) (SD)	MEAN (n=252) (SD)
AGE (years)	56.52 (±12.1)	52.29(±13.2)	55.11(±12.93)

Total Cases-252

Sex ratio (males: females)-3:1

Mean age: 55.11 years ± 12.93 years

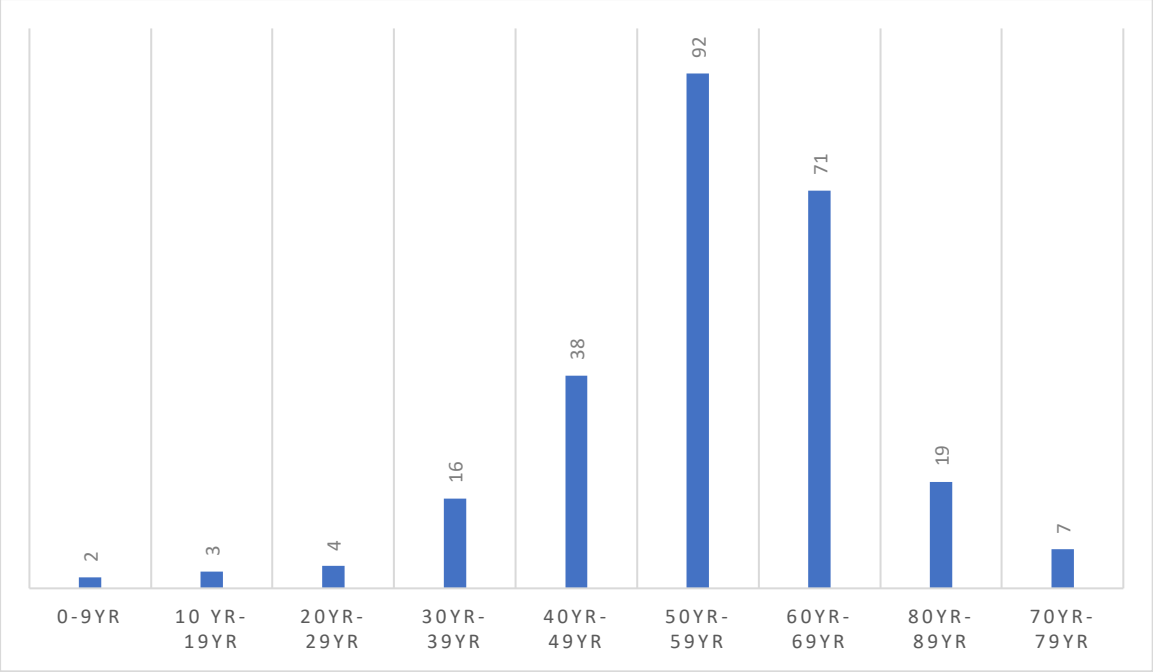

Figure 4: Age distribution in the study population

The majority of patients were in the 50-59 years group(36%) and 60-69 years(28%).

Table 2: Comorbidities in the study population

VARIABLE	**n=252 (%)**
Diabetes Mellitus	143(56.7%)
Hypertension	132(52.3%)
Dyslipidemia	115(45.6%)
Smoking	71(28.1%)
Past H/O Heart Failure	104(41.2%)
H/O Atrial Fibrillation	18(7.1%)
H/O Ventricular Tachycardia	59(23.4%)
H/O Complete Heart Block	54(21.4%)

Diabetes mellitus was the most commonly seen comorbidity in the study population with an overall prevalence of 52.3%, followed by hypertension 52.3% and dyslipidemia 45.6%. 41.2% had a history of heart failure. History of ventricular tachycardia in 23.4%, and complete heart block in 21.4%.

Table 3: Baseline Patient characteristics

VARIABLE		n=41 (%) and (mean±SD)
TYPE OF DEVICE	CRT-P	152 (60.3%)
	CRT-D	16 (39.6%)
ISCHEMIC/NON-ISCHEMIC	NON-ISCHEMIC	171(67.8%)
	ISCHEMIC	81(32.1%)
NYHA FUNCTIONAL CLASS		II-47 (18.6%)
		III-181(71.8%)
		IV-24(9.5%)
Pro BNP		150(3039±3160)
6-minute walk test(6MWT)		32(355±134)

CRT-D- cardiac resynchronization therapy-defibrillator, CRT-P-cardiac resynchronization therapy-pacemaker, NYHA- New York heart association

CRT-P implantation was done in 60.3%, and CRT-D was implanted in 39.6%. Non-ischemic heart disease as the etiology was seen 67.8%and ischemic etiology in 32.1%. Predominantly patients were in NYHA FC III (71.8%) during device implantation. Baseline Pro BNP was 3039±3160, 6MWT is 355±134 minutes at baseline. (Table 3)

Table 4: ECG findings

VARIABLE		N and mean±SD
QRSd (ms)		167±24
PR prolongation n(%)		78(30.9%)
Bundle branch block	LBBB n(%)	227(90.07%)
	RBBB n(%)	16(6.3%)
	IVCD(%)	9(3.5%)

QRSd-QRS duration, LBBB-Left bundle branch block, RBBB-Right bundle branch block, IVCD- interventricular defect

The study population had a mean QRS duration of 167ms with a standard deviation of ±24ms. 90.07% of patients had left bundle branch block, and right bundle branch block was seen 6.3%. PR interval was prolonged in 30.9%.

Table 5: Echocardiographic parameters

VARIABLE		mean±SD
LVIDS (mm)		65.62 (10.06)
LVIDD (mm)		54.45 (10.58)
LVEF (%)		29.46 (8.26)
ESV(ml) n=141		193.52 (67.14)
EDV(ml) n=143		139.58 (55.22)
SPWD(ms) n=122		192.98 (89.54)
Interventricular delay(ms) n=68		58(29)
Mitral Regurgitation	Trivial n (%)	35 (18.2%)
	Mild n (%)	76 (39.6%)
	Moderate n (%)	60 (31.2%)
	Severe n (%)	10 (5.2%)
RV dysfunction		19 (7.53%)

LVEF- left ventricular ejection fraction, ESV-end systolic volume, EDV-end-diastolic volume, LVIDD-LV internal diameter in diastole, LVIDS-LV internal diameter in systole, SPWP-septum to posterior wall delay,

. Mild and moderate mitral regurgitation was found in 39.6% and 31.2%, respectively. Severe mitral regurgitation The echocardiographic parameters at the baseline showed mean LV internal diameter during diastole of 65.62mm, LV internal diameter during systole54.49mm, and mean LV ejection fraction was 29.46%. The mean end-systolic volume in baseline was 193.52ml, end-diastolic volume was 139.58ml. Markers of dyssynchrony, mean septum to

posterior wall delay was 192.98ms, whereas interventricular delay was 58ms was present in 5.2% at baseline. Right ventricular dysfunction was present in 7.53% of patients.

Table 6: Hemodynamic parameters

Variable	Mean ± SD
Pulmonary capillary wedge pressure(mmHg) n=69	20±8.3
Left ventricular end-diastolic pressure(mmHg) n=76	21±8
Mean Pulmonary arterial pressure (mmHg) n=71	29±10

Hemodynamic data were available in 76 patients. The mean pulmonary capillary wedge pressure was 20mmHg, LV end-diastolic pressure was 21mmHg, and mean pulmonary artery pressure was 29mmHg.

Table 7 : MRI parameters

Variable		N=65(SD)
LVESV (ml)		143±70
LVEDV (ml)		111±66
LVEF (%)		24±9.3
LGE n (%)	Absent	36(55.38%)
	Present	29(44.6%)
	Transmural	18(27.69%)
	Subendocardial	6(9.2%)
	Mid-myocardial	5(7.6%)

LGE-late gadolinium enhancement, LVESV- Left ventricular end-systolic volume, LVEDV-left ventricular end-diastolic volume, LVEF-left ventricular ejection fraction

MRI data was available in 65 patients. Mean normalized LV end-systolic volume was 143ml, mean normalized LV end-diastolic volume was 111ml. The mean MRI LV ejection fraction was 24%. Late gadolinium enhancement was present in 44%, whereas it was not present in 55%. The most common pattern of enhancement was transmural(27.69%), followed by subendocardial (9.2%) and mid-myocardial in 7.6%

Table 8: Medication History

VARIABLE	N (%)
LOOP DIURETICS	241(95.6%)
MRA	226(89.6%)
BETA-BLOCKERS	231(91.6%)
ACAI	142(56.3%)
ARB	69(27.3%)
DIGOXIN	149(59.1%)
AMIODARONE	62(24.6%)
ARNI	149(59.1%)

MRA-Mineralocorticoid receptor antagonist, ACEI- Angiotensin-converting enzyme Inhibitor, ARB-Angiotensin receptor blocker, ARNI- Angiotensin receptor neprilysin inhibitor

The study population was on loop diuretics in 95.6%, mineralocorticoid antagonist in 89%, beta-blockers in 91%, angiotensin-converting enzyme inhibitors in 56.3%, angiotensin receptor blocker in 27.3%, digoxin in 59%, amiodarone in 24.6%, and angiotensin receptor neprilysin inhibitor in 59.1%.

Analysis of change in parameters in follow-up.

Table 9: Change in NYHA Class Over Time (n = 250)

NYHA Class		Baseline					Stuart-Maxwell test	
		I	II	III	IV	Total	χ2	P Value
Follow-Up	I	0 (0.0%)	4 (1.6%)	14 (5.6%)	1 (0.4%)	19 (7.6%)	154.971	<0.001
	II	0 (0.0%)	39 (15.6%)	136 (54.4%)	14 (5.6%)	189 (75.6%)		
	III	0 (0.0%)	3 (1.2%)	28 (11.2%)	7 (2.8%)	38 (15.2%)		
	IV	0 (0.0%)	1 (0.4%)	3 (1.2%)	0 (0.0%)	4 (1.6%)		
	Total	0 (0.0%)	47 (18.8%)	181 (72.4%)	22 (8.8%)	250 (100.0%)		

The uncolored cells on the diagonal represent patients whose category did not change. The red shaded cells represent patients who moved to a lower category. The green shaded cells represent patients who moved to a higher category.

Stuart-Maxwell test was used to assess the change in NYHA Class between the two time points. A significant result denotes that the distribution of patients in terms of NYHA Class changed significantly over time.

The changes observed in NYHA Class over time were as follows:

4 (1.6%) patients moved from the category NYHA Class: II to the category I. 3 (1.2%) patients moved from the category NYHA Class: II to the category III. 1 (0.4%) patients moved from the category NYHA Class: II to the category IV. 14 (5.6%) patients moved from the category NYHA Class: III to the category I. 136 (54.4%) patients moved from the category NYHA Class: III to the category II. 3 (1.2%) patients moved from the category NYHA Class: III to the category IV. 1 (0.4%) patients moved from the category NYHA Class: IV to the category I. 14 (5.6%) patients moved from the category NYHA Class: IV to the category II. 7 (2.8%) patients moved from the category NYHA Class: IV to the category III.

The overall change in NYHA Class was statistically significant (Stuart-Maxwell test: $\chi 2 = 154.971$, $p = <0.001$)

Table 10: Assessment of change in QRSd (ms) over time (n = 249)

Timepoint	QRSd (ms)			Wilcoxon Test	
	Mean (SD)	Median (IQR)	Range	V	P-Value
Baseline	167.99 (24.10)	160.00 (20.00)	100.00 - 260.00	25533.0	<0.001
Follow-Up	131.31 (15.77)	130.00 (20.00)	110.00 - 200.00		
Absolute Change	-36.86 (28.38)	-40.00 (40.00)	-110.00 - 50.00		
Percent Change	-20.4% (14.5)	-23.5% (19.5)	-48% - 38%		

Non-parametric tests were used to make a statistical inference as data were not normally distributed. Paired Wilcoxon test was used to explore the difference in QRSd (ms) at the two time points.

The mean QRSd (ms) decreased from a maximum of 167.99 at the Baseline timepoint to a minimum of 131.31 at the Follow-Up timepoint. This change was statistically significant (Wilcoxon Test: V = 25533.0, p = <0.001).

Table 11: Assessment of change in LVIDd over time (n = 249)

Timepoint	LVIDd			Wilcoxon Test	
	Mean (SD)	Median (IQR)	Range	V	P-Value
Baseline	65.62 (10.06)	65.00 (11.25)	16.00 - 106.00	12527.5	<0.001
Follow-Up	62.73 (10.22)	62.00 (14.00)	35.00 - 90.00		
Absolute Change	-3.10 (8.65)	-1.00 (4.00)	-37.00 - 23.00		
Percent Change	-4.1% (12.7)	-1.5% (6.7)	-48% - 46%		

Non-parametric tests were used to make a statistical inference as data were not normally distributed. Paired Wilcoxon test was used to explore the difference in LVIDd at the two time points.

The mean LVIDd decreased from a maximum of 65.62 at the Baseline timepoint to a minimum of 62.73 at the Follow-Up timepoint. This change was statistically significant (Wilcoxon Test: V = 12527.5, p = <0.001).

Table 12: Assessment of change in LVIDs over time (n = 249)

Timepoint	LVIDs			Wilcoxon Test	
	Mean (SD)	Median (IQR)	Range	V	P-Value
Baseline	54.45 (10.58)	54.00 (13.25)	12.00 - 98.00	17646.0	<0.001
Follow-Up	50.57 (11.02)	50.00 (14.00)	20.00 - 82.00		
Absolute Change	-4.06 (9.53)	-2.00 (5.00)	-37.00 - 39.00		
Percent Change	-6.3% (18.7)	-3.6% (9.6)	-65% - 144%		

Non-parametric tests were used to make a statistical inference as data were not normally distributed. Paired Wilcoxon test was used to explore the difference in LVIDs at the two time points.

The mean LVIDs decreased from a maximum of 54.45 at the Baseline timepoint to a minimum of 50.57 at the Follow-Up timepoint. This change was statistically significant (Wilcoxon Test: V = 17646.0, p = <0.001).

Table 13: Assessment of change in LVEF (%) over time (n = 249)

Timepoint	LVEF (%)			Wilcoxon Test	
	Mean (SD)	Median (IQR)	Range	V	P-Value
Baseline	29.46 (8.26)	29.00 (10.00)	10.00 - 64.00	2540.5	<0.001
Follow-Up	37.07 (9.36)	36.00 (9.00)	15.00 - 65.00		
Absolute Change	7.61 (9.46)	6.00 (9.00)	-20.00 - 38.00		
Percent Change	32.4% (42.1)	22.2% (44.7)	-52% - 260%		

Non-parametric tests were used to make a statistical inference as data were not normally distributed. Paired Wilcoxon test was used to explore the difference in LVEF (%) at the two time points.

The mean LVEF (%) increased from a minimum of 29.46 at the Baseline timepoint to a maximum of 37.07 at the Follow-Up timepoint. This change was statistically significant (Wilcoxon Test: V = 2540.5, p = <0.001).

Table 14: Assessment of change in EDV (mL) over time (n = 17)

Timepoint	EDV (mL)			Wilcoxon Test	
	Mean (SD)	Median (IQR)	Range	V	P-Value
Baseline	193.52 (67.14)	180.00 (79.00)	70.00 - 422.00	114.0	0.019
Follow-Up	189.38 (96.62)	185.50 (124.50)	80.00 - 500.00		
Absolute Change	-53.53 (76.98)	-43.00 (102.00)	-201.00 - 56.00		
Percent Change	-21.1% (27.3)	-26.1% (34.5)	-71% - 25%		

Non-parametric tests were used to make a statistical inference as data were not normally distributed. Paired Wilcoxon test was used to explore the difference in EDV (mL) at the two time points.

The mean EDV (mL) decreased from a maximum of 193.52 at the Baseline timepoint to a minimum of 189.38 at the Follow-Up timepoint. This change was statistically significant (Wilcoxon Test: V = 114.0, p = 0.019).

Table 15: Assessment of change in ESV (mL) over time (n = 17)

Timepoint	ESV (mL)			Wilcoxon Test	
	Mean (SD)	Median (IQR)	Range	V	P-Value
Baseline	139.58 (55.22)	125.50 (72.00)	38.00 - 315.00	124.0	0.004
Follow-Up	125.38 (84.52)	121.00 (89.50)	33.00 - 450.00		
Absolute Change	-54.35 (58.88)	-53.00 (60.00)	-153.00 - 52.00		
Percent Change	-30.7% (30.7)	-36.5% (37.9)	-81% - 39%		

Non-parametric tests were used to make a statistical inference as data were not normally distributed. Paired Wilcoxon test was used to explore the difference in ESV (mL) at the two time points.

The mean ESV (mL) decreased from a maximum of 139.58 at the Baseline timepoint to a minimum of 125.38 at the Follow-Up timepoint. This change was statistically significant (Wilcoxon Test: V = 124.0, p = 0.004).

Table 16: Change in MR Over Time (n = 192)

MR		Baseline						Stuart-Maxwell test	
		Absent	Trivial	Mild	Moderate	Severe	Total	χ2	P Value
Follow-Up	Absent	3 (1.6%)	2 (1.0%)	4 (2.1%)	4 (2.1%)	1 (0.5%)	14 (7.3%)	50.904	<0.001
	Trivial	4 (2.1%)	25 (13.0%)	39 (20.3%)	20 (10.4%)	2 (1.0%)	90 (46.9%)		
	Mild	3 (1.6%)	6 (3.1%)	24 (12.5%)	24 (12.5%)	1 (0.5%)	58 (30.2%)		
	Moderate	0 (0.0%)	0 (0.0%)	8 (4.2%)	10 (5.2%)	5 (2.6%)	23 (12.0%)		
	Severe	1 (0.5%)	2 (1.0%)	1 (0.5%)	2 (1.0%)	1 (0.5%)	7 (3.6%)		
	Total	11 (5.7%)	35 (18.2%)	76 (39.6%)	60 (31.2%)	10 (5.2%)	192 (100.0%)		

The uncolored cells on the diagonal represent patients whose category did not change. The red shaded cells represent patients who moved to a lower category. The green shaded cells represent patients who moved to a higher category.

Stuart-Maxwell test was used to assess the change in MR between the two time points. A significant result denotes that the distribution of patients in terms of MR changed significantly over time.

The changes observed in MR over time were as follows:

4 (2.1%) patients moved from the category MR: Absent to the category Trivial. 3 (1.6%) patients moved from the category MR: Absent to the category Mild. 1 (0.5%) patients moved from the category MR: Absent to the category Severe. 2 (1.0%) patients moved from the category MR: Trivial to the category Absent. 6 (3.1%) patients moved from the category MR: Trivial to the category Mild. 2 (1.0%) patients moved from the category MR: Trivial to the category Severe. 4 (2.1%) patients moved from the category MR: Mild to the category Absent.

39 (20.3%) patients moved from the category MR: Mild to the category Trivial. 8 (4.2%) patients moved from the category MR: Mild to the category Moderate. 1 (0.5%) patients moved from the category MR: Mild to the category Severe. 4 (2.1%) patients moved from the category MR: Moderate to the category Absent. 20 (10.4%) patients moved from the category MR: Moderate to the category Trivial. 24 (12.5%) patients moved from the category MR: Moderate to the category Mild. 2 (1.0%) patients moved from the category MR: Moderate to the category Severe. 1 (0.5%) patients moved from the category MR: Severe to the category Absent. 2 (1.0%) patients moved from the category MR: Severe to the category Trivial. 1 (0.5%) patients moved from the category MR: Severe to the category Mild. 5 (2.6%) patients moved from the category MR: Severe to the category Moderate.

The overall change in MR was statistically significant (Stuart-Maxwell test: $\chi 2 = 50.904$, $p = <0.001$)

Comparison of parameters between CRT-D and CRT-P

Table 17: Association between Device Used and Parameters

Parameters	Device Used		p-value
	CRT-D (n = 100)	CRT-P (n = 152)	
Age (Years)* **	58.52 ± 10.73	53.72 ± 13.92	0.003[1]
Gender* **			<0.001[2]
Male	87 (87.0%)	102 (67.1%)	
Female	13 (13.0%)	50 (32.9%)	
Type of Cardiomyopathy* **			<0.001[2]
Ischemic	53 (53.0%)	28 (18.4%)	
Non ischemic	47 (47.0%)	124 (81.6%)	
NYHA Class (Baseline)* **			0.009[2]
II	10 (10.0%)	37 (24.3%)	
III	77 (77.0%)	104 (68.4%)	
IV	13 (13.0%)	11 (7.2%)	
DM (Yes)* **	68 (68.0%)	75 (49.3%)	0.003[2]
HTN (Yes)* **	66 (66.0%)	66 (43.4%)	<0.001[2]
Dyslipidemia (Yes)* **	58 (58.0%)	57 (37.5%)	0.001[2]
Smoking (Yes)* **	39 (39.0%)	32 (21.1%)	0.002[2]
P/H/O Heart Failure (Yes)	44 (44.0%)	60 (39.5%)	0.475[2]
Atrial Fibrillation (Baseline) (Yes)* **	3 (3.0%)	15 (9.9%)	0.038[2]
VT/NSVT (Yes)* **	56 (56.0%)	3 (2.0%)	<0.001[2]
CHB (Yes)* **	12 (12.0%)	42 (27.6%)	0.003[2]
Heart Rate (BPM) (Baseline)	73.07 ± 9.21	72.50 ± 10.36	0.989[1]
QRSd (ms) (Baseline)	171.56 ± 24.63	165.64 ± 23.54	0.058[1]
QRSd (Baseline)			0.090[2]
<150 ms	9 (9.0%)	25 (16.4%)	
≥150 ms	91 (91.0%)	127 (83.6%)	
Bundle Branch Block			0.153[2]
Atypical	6 (6.0%)	3 (2.0%)	
Left	86 (86.0%)	141 (92.8%)	
Right	8 (8.0%)	8 (5.3%)	
Baseline QRS Axis* **			0.049[3]
LAD	96 (97.0%)	135 (88.8%)	
Normal	2 (2.0%)	14 (9.2%)	
RAD	1 (1.0%)	3 (2.0%)	
Prolonged PR (Yes)	38 (44.2%)	40 (32.3%)	0.079[2]
NT-Pro BPN (pg/mL) (Baseline)	2953.43 ± 3087.00	3066.04 ± 3214.39	0.969[1]
6MWT (m)	304.60 ± 138.60	379.05 ± 129.69	0.170[4]
LVIDd (Baseline)	66.57 ± 9.94	65.00 ± 10.13	0.206[1]
LVIDs (Baseline)	55.13 ± 10.62	54.01 ± 10.57	0.483[1]
LVEF (%) (Baseline)	29.31 ± 8.17	29.57 ± 8.35	0.784[1]
EDV (mL) (Baseline)	201.69 ± 63.60	188.90 ± 68.99	0.131[1]
ESV (mL) (Baseline)	144.10 ± 55.31	136.98 ± 55.31	0.446[1]

Parameters	Device Used		p-value
	CRT-D (n = 100)	CRT-P (n = 152)	
SPWD (ms) (Baseline)	184.24 ± 108.51	196.94 ± 79.93	0.222[1]
Interventricular delay (ms)	58.85 ± 29.58	59.04 ± 29.30	0.981[4]
IVS Thickness (mm) (Baseline)	8.87 ± 2.63	8.93 ± 2.63	0.923[1]
Posterior Wall Thickness (mm) (Baseline)	10.08 ± 2.63	11.03 ± 13.27	0.536[1]
MR (Baseline)			0.203[2]
Absent	5 (5.1%)	10 (6.8%)	
Trivial	15 (15.2%)	31 (21.1%)	
Mild	37 (37.4%)	61 (41.5%)	
Moderate	38 (38.4%)	36 (24.5%)	
Severe	4 (4.0%)	9 (6.1%)	
RV Dysfunction (Baseline) (Yes)	9 (9.0%)	10 (6.6%)	0.476[2]
Loop Diuretic (Baseline) (Yes)	95 (95.0%)	146 (96.1%)	0.757[3]
MRA (Baseline) (Yes)	91 (91.0%)	135 (88.8%)	0.577[2]
Beta-Blocker (Baseline) (Yes)	94 (94.0%)	137 (90.1%)	0.277[2]
ARB (Baseline) (Yes)	29 (29.0%)	40 (26.3%)	0.640[2]
ARNI (Baseline) (Yes)	5 (5.0%)	3 (2.0%)	0.271[3]
ACE Inhibitor (Baseline) (Yes)	50 (50.0%)	92 (60.5%)	0.099[2]
Digoxin (Yes)	56 (56.0%)	93 (61.2%)	0.413[2]
Amiodarone (Yes)	31 (31.0%)	31 (20.4%)	0.056[2]
MRI LV EDV Absolute (mL)	264.00 ± 121.32	227.17 ± 115.62	0.143[1]
MRI LV EDV Normalized (mL)	153.70 ± 76.13	138.09 ± 68.31	0.540[1]
MRI LV ESV Absolute (mL)	215.67 ± 114.12	171.69 ± 108.56	0.054[1]
MRI LV ESV Normalized (mL)	124.35 ± 71.47	104.71 ± 64.25	0.221[1]
MRI LVEF (%)* **	19.73 ± 7.59	26.47 ± 9.46	0.004[4]
MRI RWMA* **			0.003[3]
Nil	1 (4.5%)	4 (10.5%)	
Global	14 (63.6%)	33 (86.8%)	
Anterior Wall	6 (27.3%)	0 (0.0%)	
Septum	1 (4.5%)	1 (2.6%)	
MRI LGE* **			<0.001[3]
Nil	5 (20.0%)	31 (77.5%)	
Transmural	15 (60.0%)	3 (7.5%)	
Mid-Myocardial	2 (8.0%)	3 (7.5%)	
Subendocardial	3 (12.0%)	3 (7.5%)	
PCWP (mmHg)	22.48 ± 9.25	20.17 ± 7.87	0.312[4]
LV EDP (mmHg)	22.89 ± 7.83	20.00 ± 7.33	0.122[4]
MAP (mmHg)	32.62 ± 12.30	28.51 ± 9.84	0.163[4]
QLV Time (ms)	137.80 ± 38.04	150.93 ± 34.83	0.393[4]
LV Lead Position			0.465[3]
PLV	77 (77.8%)	107 (70.9%)	
Lateral	18 (18.2%)	31 (20.5%)	
Epicardial	2 (2.0%)	10 (6.6%)	
MCV	1 (1.0%)	2 (1.3%)	
ALV	1 (1.0%)	1 (0.7%)	
Response (Present)	57 (57.0%)	96 (63.2%)	0.327[2]
Mortality (Present)	24 (24.0%)	35 (23.0%)	0.858[2]

****Significant at p<0.05, 1: Wilcoxon-Mann-Whitney U Test, 2: Chi-Squared Test, 3: Fisher's Exact Test, 4: t-test*

These are the statistically significant parameters in the analysis of patients with CRT-D vs CRT-P

Table 18: Statistically significant parameters while comparing CRT-D vs CRT-P

Variable	CRT-D	CRT- P	P-value
Age (Years)* **	58.52 ± 10.73	53.72 ± 13.92	0.003[1]
Gender* **			<0.001[2]
Male	87 (87.0%)	102 (67.1%)	
Female	13 (13.0%)	50 (32.9%)	
Type of Cardiomyopathy* **			<0.001[2]
Ischemic	53 (53.0%)	28 (18.4%)	
Non ischemic	47 (47.0%)	124 (81.6%)	
NYHA Class (Baseline)* **			0.009[2]
II	10 (10.0%)	37 (24.3%)	
III	77 (77.0%)	104 (68.4%)	
IV	13 (13.0%)	11 (7.2%)	
DM (Yes)* **	68 (68.0%)	75 (49.3%)	0.003[2]
HTN (Yes)* **	66 (66.0%)	66 (43.4%)	<0.001[2]
Dyslipidemia (Yes)* **	58 (58.0%)	57 (37.5%)	0.001[2]
Smoking (Yes)* **	39 (39.0%)	32 (21.1%)	0.002[2]
Atrial Fibrillation (Baseline) (Yes)* **	3 (3.0%)	15 (9.9%)	0.038[2]
VT/NSVT (Yes)* **	56 (56.0%)	3 (2.0%)	<0.001[2]
CHB (Yes)* **	12 (12.0%)	42 (27.6%)	0.003[2]
MRI LVEF (%)* **	19.73 ± 7.59	26.47 ± 9.46	0.004[4]

Patients in the CRT-D group were relatively elder, with a mean age of 58.52 years when compared to patients in the CRT-P group, where the mean age was 53.72 years(p=0.003). The type of device implanted in males and females was significantly different, as more CRT-D devices being implanted in males (87%) as compared to females (13%), whereas CRT -P was implanted in 67.1% of males and 32.9% in females(p=0.001). The proportion of comorbidities was more in the CRT-D group, like DM(68%), hypertension (66%), dyslipidemia(58%), smoking(39%) when compared with patients in the CRT-P group(DM 49%, hypertension 43%, Dyslipidemia 37%, smoking 21%). Ischemic etiology of cardiomyopathy was seen in 53% of patients in the CRT-D group, whereas it was 18.4% in the CRT-P group. The proportion of nonischemic etiology was more in the CRT-P group, 81.6%, whereas it was 47% in the CRT-D group($p<0.001$). The prevalence of atrial fibrillation in CRT- D was 3% when compared with the CRT-P group, where it was 9.9% (p=0.038). History of VT was found in 56% of patients in the CRT-D group, whereas it was found in 2% of participants in the CRT-P group (p=0.001). The prevalence of CHB was more in CRT-P(12%) group than CRT-D(27.6%) group(p=0.03). LVEF on MRI was found to be 19.73% in the CRT-D group of patients, whereas it was 26.47% in the CRT-P group (0.004)

These are some of the important statistically **not** significant parameters in the analysis of patients with CRT-D vs CRT-P.

Table 19: Statistically nonsignificant parameters while comparing CRT-D vs CRT-P

Variable	CRT-D	CRT-P	P-value
P/H/O Heart Failure (Yes)	44 (44.0%)	60 (39.5%)	0.475[2]
QRSd (ms) (Baseline)	171.56 ± 24.63	165.64 ± 23.54	0.058[1]
QRSd (Baseline)			0.090[2]
<150 ms	9 (9.0%)	25 (16.4%)	
≥150 ms	91 (91.0%)	127 (83.6%)	
Bundle Branch Block			0.153[2]
Atypical	6 (6.0%)	3 (2.0%)	
Left	86 (86.0%)	141 (92.8%)	
Right	8 (8.0%)	8 (5.3%)	
LVIDd (Baseline)	66.57 ± 9.94	65.00 ± 10.13	0.206[1]
LVIDs (Baseline)	55.13 ± 10.62	54.01 ± 10.57	0.483[1]
LVEF (%) (Baseline)	29.31 ± 8.17	29.57 ± 8.35	0.784[1]
EDV (mL) (Baseline)	201.69 ± 63.60	188.90 ± 68.99	0.131[1]
ESV (mL) (Baseline)	144.10 ± 55.31	136.98 ± 55.31	0.446[1]
SPWD (ms) (Baseline)	184.24 ± 108.51	196.94 ± 79.93	0.222[1]
Interventricular delay (ms)	58.85 ± 29.58	59.04 ± 29.30	0.981[4]
QLD Time (ms)	137.80 ± 38.04	150.93 ± 34.83	0.393[4]
LV Lead Position			0.465[3]
PLV	77 (77.8%)	107 (70.9%)	
Lateral	18 (18.2%)	31 (20.5%)	
Epicardial	2 (2.0%)	10 (6.6%)	
MCV	1 (1.0%)	2 (1.3%)	
ALV	1 (1.0%)	1 (0.7%)	
Response (Present)	57 (57.0%)	96 (63.2%)	0.327[2]
Mortality (Present)	24 (24.0%)	35 (23.0%)	0.858[2]

The mean QRS duration in the CRT-D group was 171.56ms which was higher than the QRS duration in the CRT-P group(165.64ms), but it was statistically not significant(p=0.058). Around 86% of patients in CRT-D and 99.2% patients had left bundle branch block at baseline, not statistically significant (p=0.15). Past history of HF was found in 44% of patients with CRT-D group, whereas it was found in 39% in CRT-P group (p=0.75). The mean QLV time in CRT-D and CRT-P groups was 137.8ms and 150.93ms, respectively, but this difference was not statistically significant (p=0.393). Lead was placed in posterolateral branch in 77.8% and 70.9% in CRT-D and CRT-P group of patients, respectively, but this finding was not statistically different (p=0.465). Response to CRT was present in 57% and 63.2% in CRT-D and CRT-P group of patients; respectively, though the response rate was more in the CRT-P group when compared with the CRT-D group, this was statistically not significant. All-cause mortality was found in 24%, and 23% in CRT-D and CRT-P groups of patients, respectively, which was similar in both the groups and it was not statistically significant.

Comparison of parameters in responders and non-responders

Table 20:Analysis of parameters between Responders and non-responders

Parameters	Response		p-value
	Present (n = 153)	Absent (n = 99)	
Age (Years)	56.33 ± 12.04	54.53 ± 14.21	0.478[1]
Gender			0.602[2]
Male	113 (73.9%)	76 (76.8%)	
Female	40 (26.1%)	23 (23.2%)	
Device Used			0.327[2]
CRT-D	57 (37.3%)	43 (43.4%)	
CRT-P	96 (62.7%)	56 (56.6%)	
Type of Cardiomyopathy			0.380[2]
Ischemic	46 (30.1%)	35 (35.4%)	
Non-ischemic	107 (69.9%)	64 (64.6%)	
NYHA Class (Baseline)			0.311[2]
II	26 (17.0%)	21 (21.2%)	
III	115 (75.2%)	66 (66.7%)	
IV	12 (7.8%)	12 (12.1%)	
DM (Yes)	89 (58.2%)	54 (54.5%)	0.571[2]
HTN (Yes)	80 (52.3%)	52 (52.5%)	0.971[2]
Dyslipidemia (Yes)	65 (42.5%)	50 (50.5%)	0.212[2]
Smoking (Yes)* **	35 (22.9%)	36 (36.4%)	0.020[2]
P/H/O Heart Failure (Yes)	59 (38.6%)	45 (45.5%)	0.278[2]
Atrial Fibrillation (Baseline) (Yes)* **	7 (4.6%)	11 (11.1%)	0.049[2]
VT/NSVT (Yes)* **	29 (19.0%)	30 (30.3%)	0.038[2]
CHB (Yes)* **	26 (17.0%)	28 (28.3%)	0.033[2]
Heart Rate (BPM) (Baseline)	73.21 ± 8.75	71.98 ± 11.48	0.689[1]
QRSd (ms) (Baseline)* **	171.19 ± 23.34	163.05 ± 24.55	0.009[1]
QRSd (Baseline)* **			0.012[2]
<150 ms	14 (9.2%)	20 (20.2%)	
≥150 ms	139 (90.8%)	79 (79.8%)	
Bundle Branch Block			0.376[2]
Atypical	4 (2.6%)	5 (5.1%)	
Left	141 (92.2%)	86 (86.9%)	
Right	8 (5.2%)	8 (8.1%)	
Baseline QRS Axis			0.788[3]
LAD	142 (92.8%)	89 (90.8%)	
Normal	9 (5.9%)	7 (7.1%)	
RAD	2 (1.3%)	2 (2.0%)	
Prolonged PR (Yes)	48 (36.4%)	30 (38.5%)	0.761[2]
NT-Pro BPN (pg/mL) (Baseline)	2972.72 ± 3168.16	3100.86 ± 3162.92	0.743[1]
6MWT (m)	337.76 ± 139.42	390.18 ± 124.74	0.290[4]
LVIDd (Baseline)	66.40 ± 9.34	64.42 ± 11.04	0.112[1]
LVIDs (Baseline)* **	55.53 ± 9.45	52.79 ± 11.99	0.035[1]
LVEF (%) (Baseline)* **	27.03 ± 6.12	33.22 ± 9.65	<0.001[4]

Parameters	Response		p-value
	Present (n = 153)	Absent (n = 99)	
EDV (mL) (Baseline)	199.45 ± 68.12	183.68 ± 64.94	0.167[1]
ESV (mL) (Baseline)	146.00 ± 54.41	128.81 ± 55.39	0.055[1]
SPWD (ms) (Baseline)	194.23 ± 88.15	190.51 ± 93.28	0.591[1]
Interventricular delay (ms)	61.11 ± 27.55	54.83 ± 32.32	0.431[4]
IVS Thickness (mm) (Baseline)	8.93 ± 2.49	8.87 ± 2.87	0.514[1]
Posterior Wall Thickness (mm) (Baseline)	11.18 ± 12.80	9.69 ± 2.75	0.208[1]
MR (Baseline)			0.937[2]
Absent	10 (6.7%)	5 (5.2%)	
Trivial	26 (17.3%)	20 (20.8%)	
Mild	59 (39.3%)	39 (40.6%)	
Moderate	47 (31.3%)	27 (28.1%)	
Severe	8 (5.3%)	5 (5.2%)	
RV Dysfunction (Baseline) (Yes)	11 (7.2%)	8 (8.1%)	0.794[2]
Loop Diuretic (Baseline) (Yes)	148 (96.7%)	93 (93.9%)	0.350[3]
MRA (Baseline) (Yes)	141 (92.2%)	85 (85.9%)	0.108[2]
Beta-Blocker (Baseline) (Yes)	143 (93.5%)	88 (88.9%)	0.199[2]
ARB (Baseline) (Yes)	41 (26.8%)	28 (28.3%)	0.796[2]
ARNI (Baseline) (Yes)	4 (2.6%)	4 (4.0%)	0.715[3]
ACE Inhibitor (Baseline) (Yes)	88 (57.5%)	54 (54.5%)	0.642[2]
Digoxin (Yes)	90 (58.8%)	59 (59.6%)	0.903[2]
Amiodarone (Yes)	33 (21.6%)	29 (29.3%)	0.164[2]
MRI LV EDV Absolute (mL)	246.26 ± 94.15	228.78 ± 160.81	0.061[1]
MRI LV EDV Normalized (mL)	145.55 ± 52.09	139.76 ± 103.41	0.051[1]
MRI LV ESV Absolute (mL)* **	194.21 ± 85.67	174.22 ± 156.20	0.031[1]
MRI LV ESV Normalized (mL)* **	113.53 ± 47.45	108.12 ± 99.59	0.043[1]
MRI LVEF (%)	22.32 ± 8.59	27.44 ± 10.19	0.054[1]
MRI RWMA			0.237[3]
Nil	4 (9.8%)	1 (5.3%)	
Global	33 (80.5%)	14 (73.7%)	
Anterior Wall	4 (9.8%)	2 (10.5%)	
Septum	0 (0.0%)	2 (10.5%)	
MRI LGE			0.477[3]
Nil	27 (61.4%)	9 (42.9%)	
Transmural	11 (25.0%)	7 (33.3%)	
Mid-Myocardial	3 (6.8%)	2 (9.5%)	
Subendocardial	3 (6.8%)	3 (14.3%)	
PCWP (mmHg)	20.18 ± 8.47	21.87 ± 8.26	0.407[4]
LV EDP (mmHg)	20.49 ± 7.83	22.00 ± 7.16	0.398[4]
MAP (mmHg)	28.90 ± 11.46	31.19 ± 9.98	0.167[1]
H/O AV Nodal Ablation (Yes)	1 (0.7%)	0 (0.0%)	1.000[3]
QLD Time (ms)	149.59 ± 34.75	137.38 ± 39.47	0.468[4]
LV Lead Position			0.556[3]
PLV	116 (76.3%)	68 (69.4%)	
Lateral	28 (18.4%)	21 (21.4%)	
Epicardial	5 (3.3%)	7 (7.1%)	
MCV	2 (1.3%)	1 (1.0%)	

Parameters	Response		p-value
	Present (n = 153)	Absent (n = 99)	
ALV	1 (0.7%)	1 (1.0%)	
Active Fixation lead (Yes)	48 (53.3%)	28 (50.9%)	0.777[2]
Upgradation (Yes)	18 (11.8%)	11 (11.1%)	0.874[2]
Biventricular Pacing	97.64 ± 4.76	95.88 ± 14.95	0.224[1]
Mortality (Present)* **	18 (11.8%)	41 (41.4%)	<0.001[2]

****Significant at p<0.05, 1: Wilcoxon-Mann-Whitney U Test, 2: Chi-Squared Test, 3: Fisher's Exact Test, 4: t-test*

The following variables were found to be statistically significant in the univariate analysis of responders and non-responders.

Table 21: Statistically significant parameters while comparing responders vs non-responders

Variables	Responders	Non-responders	P-value
Smoking (Yes)* **	35 (22.9%)	36 (36.4%)	0.020[2]
Atrial Fibrillation (Baseline) (Yes)* **	7 (4.6%)	11 (11.1%)	0.049[2]
VT/NSVT (Yes)* **	29 (19.0%)	30 (30.3%)	0.038[2]
CHB (Yes)* **	26 (17.0%)	28 (28.3%)	0.033[2]
QRSd (ms) (Baseline)* **	171.19 ± 23.34	163.05 ± 24.55	0.009[1]
QRSd (Baseline)* **			0.012[2]
<150 ms	14 (9.2%)	20 (20.2%)	
≥150 ms	139 (90.8%)	79 (79.8%)	

MRI LV ESV Normalized (mL)* **	113.53 ± 47.45	108.12 ± 99.59	0.043[1]
Mortality (Present)* **	18 (11.8%)	41 (41.4%)	<0.001[2]

11.1% of the participants in the non-responders had atrial fibrillation, whereas 4.6% of the participants in the responders had Atrial Fibrillation. This was a statistically significant difference (p = 0.049). The presence of atrial fibrillation is associated with non-responders with an Odds ratio of 2.61(0.97-6.97) and relative risk of 1.63(1.2-2.6).

19.0% of the participants in the responder group had a history of VT/NSVT, whereas 30.3% of the participants in the non-responder group had VT/NSVT. There was a statistically significant difference (p = 0.038). The presence of VT/NSVT at baseline is associated with non-responders with an odds ratio of 1.86(1.03-3.35) and relative risk of 1.42(1.02-1.92).

17.0% of the participants in the responders group had CHB, and 28.3% of the participants in the non-responder group had CHB. There was a significant difference between the various groups in terms of distribution of CHB (p = 0.033). The presence of CHB at baseline is associated with non-responders with an odds ratio of 1.93(1.05-3.54) and a relative risk of 1.45(1.03-1.95).

The mean (SD) of QRSd (ms) in the responder group was 171.19 (23.34), and the mean (SD) of QRSd (ms) in the non-responders group was 163.05 (24.55). There was a significant difference between the 2 groups in terms of QRSd (ms) (p = 0.009).

90.8% of the participants in the responder group had QRSd ≥150 ms, and 79.8% of the participants in the non-responder group had QRSd ≥150 ms. This was statistically significant (p = 0.012).

The mean (SD) of LVIDs at baseline in the responder group was 55.53 (9.45), and the mean (SD) of LVIDs (Baseline) in the non-responder group was 52.79 (11.99). This was statistically significant (p = 0.035).

The mean (SD) of LVEF (%) at baseline in the responder group was 27.03 (6.12), and the mean (SD) of LVEF (%) in the non-responder group was 33.22 (9.65). This was statistically significant (p = 0.001). Strength of Association (Point-Biserial Correlation) = 0.37 (Large Effect Size).

The mean (SD) of MRI LV ESV normalized (mL) in the responder group was 113.53 (47.45), and the mean (SD) of MRI LV ESV normalized (mL) in the non-responder group was 108.12 (99.59). This was statistically significant (p = 0.043)

11.8% of the participants in the responder group had mortality, and 41.4% of the participants in the non-responder group had mortality. This difference was statistically significant (p = <0.001).

Non-responders were associated with a greater proportion of mortality when compared with the responders with an odds ratio of 5.3(2.81-9.99) and relative risk of 2.31(1.74-3.03)

Multivariate analysis of parameters for responders vs non-responders which were significant on univariate analysis

Table 22: Parameters after multivariate analysis(responders vs non-responders)

Variable	Relative risk (95% CI)	P-value
Smoking	0.75(0.58-0.97)	0.034
Atrial fibrillation	0.62(0.34-1.12)	0.623
Presence of VT	0.76 (0.57-1.01)	0.06

Presence of CHB	0.75(0.55-1.00)	0.057
QRS duration	1.54(1.02-2.34)	0.038
Mortality	0.43(0.29-0.46)	0.0001

Multivariate analysis showed the following: Presence of QRS duration >150ms at the baseline was associated with the response with a relative risk of 1.54(p 0.38). Smoking, if not present, was associated with response, probably a confounding factor associated with the general profile of the patients(relative risk 0.75,p 0.034). Mortality was less when the response to CRT was present, with a relative risk of 0.43(p 0.0001).

The following important variables were found to be statistically **not** significant in the univariate analysis of responders and non-responders.

Table 23: Important Statistically nonsignificant parameters (Responders vs non-responders)

Variables	**Responders**	**Non-responders**	**P-value**
Gender			0.602[2]
Male	113 (73.9%)	76 (76.8%)	
Female	40 (26.1%)	23 (23.2%)	
Device Used			0.327[2]
CRT-D	57 (37.3%)	43 (43.4%)	
CRT-P	96 (62.7%)	56 (56.6%)	
Type of Cardiomyopathy			0.380[2]

Ischemic	46 (30.1%)	35 (35.4%)	
Non-ischemic	107 (69.9%)	64 (64.6%)	
NYHA Class (Baseline)			0.311[2]
II	26 (17.0%)	21 (21.2%)	
III	115 (75.2%)	66 (66.7%)	
IV	12 (7.8%)	12 (12.1%)	
Bundle Branch Block			0.376[2]
Atypical	4 (2.6%)	5 (5.1%)	
Left	141 (92.2%)	86 (86.9%)	
Right	8 (5.2%)	8 (8.1%)	
P/H/O Heart Failure (Yes)	59 (38.6%)	45 (45.5%)	0.278[2]
ESV (mL) (Baseline)	146.00 ± 54.41	128.81 ± 55.39	0.055[1]
NT-Pro BPN (pg/mL) (Baseline)	2972.72 ± 3168.16	3100.86 ± 3162.92	0.743[1]
6MWT (m)	337.76 ± 139.42	390.18 ± 124.74	0.290[4]
QLV Time (ms)	149.59 ± 34.75	137.38 ± 39.47	0.468[4]
LV Lead Position			0.556[3]

The mean age of the responders was 56.33 (12.04). The mean age in the non-responders was 54.53 (14.21). There was no significant difference between the groups in terms of ($p = 0.478$).

73.9% of the participants in the responder group were male, and 26.1% of the participants were female. There was no significant difference between the various groups in terms of distribution of gender ($p = 0.602$)

37.3% of the participants in the responder group had CRT-D, and 62.7% of the participants had CRT-P. There was no significant difference between the various groups in terms of distribution of device Used (p = 0.327)

75.2% of the participants in the responder group had NYHA Class III, 7.8% of the participants had NYHA class IV, and 17.0% of the participants had NYHA class II. There was no significant difference between the various groups in terms of distribution of NYHA Class (p = 0.311).

38.6% of the participants in the responder group had a history of heart failure, 61.4% of the participants did not give a history of heart failure. There was no significant difference between the various groups in terms of distribution of P/H/O Heart Failure (p = 0.278).

92.2% of the participants in the responder group had LBBB, whereas 86.9% of the participants in the non-responder group had LBBB. This was statistically not significant (p = 0.376).

The mean (SD) of 6MWT (m) in the responder group was 337.76 (139.42), and the mean (SD) of 6MWT (m) in the non-responder group was 390.18 (124.74). This was statistically not significant (p = 0.290).

The mean (SD) of ESV (mL) in the responder group was 146.00 (54.41), and the mean (SD) of ESV (mL) in the non-responder group was 128.81 (55.39). This was statistically not significant (p = 0.055).

The mean (SD) of QLV Time (ms) in the responder group was 149.59 (34.75), and the mean (SD) of QLV Time (ms) in the non-responder group was 137.38 (39.47). This was statistically not significant (p = 0.468).

Predictors of mortality in the study population

Total allcause mortality- 59 (23.41%); 5.2 per 100 person years

Cardiovascular mortality- 45(17.85%); 3.9 per 100 person years

Non-Cardiovascular mortality- 14(5.55%); 1.23 per 100 person years

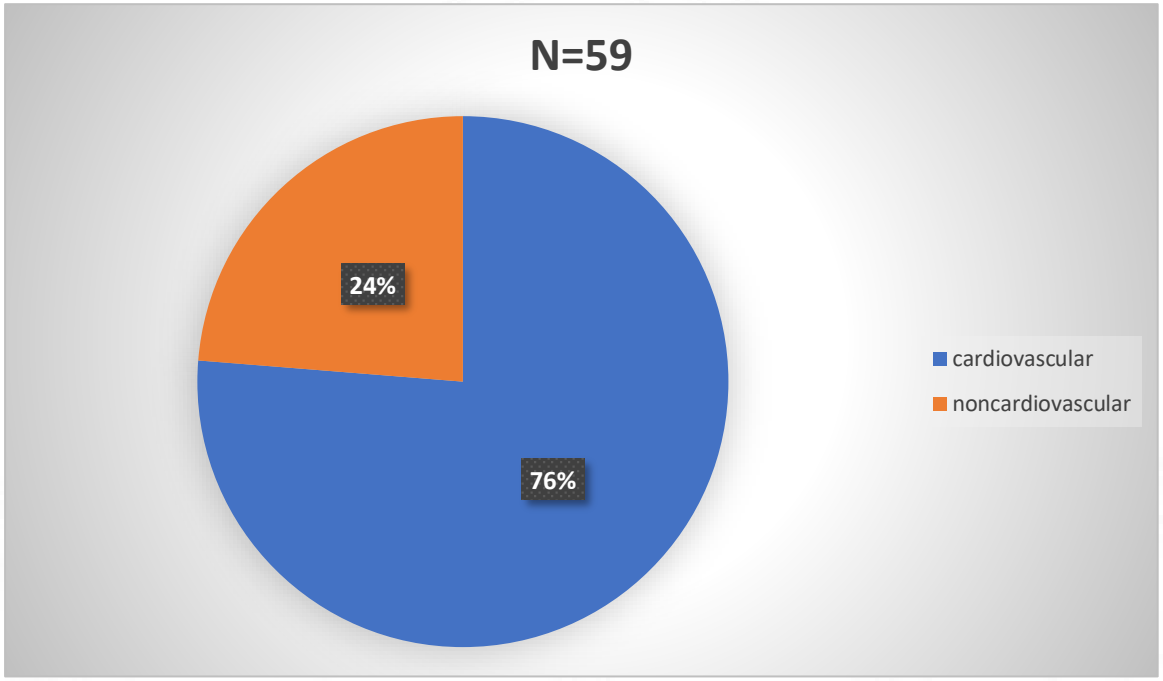

Figure 5: Distribution of etiology of mortality

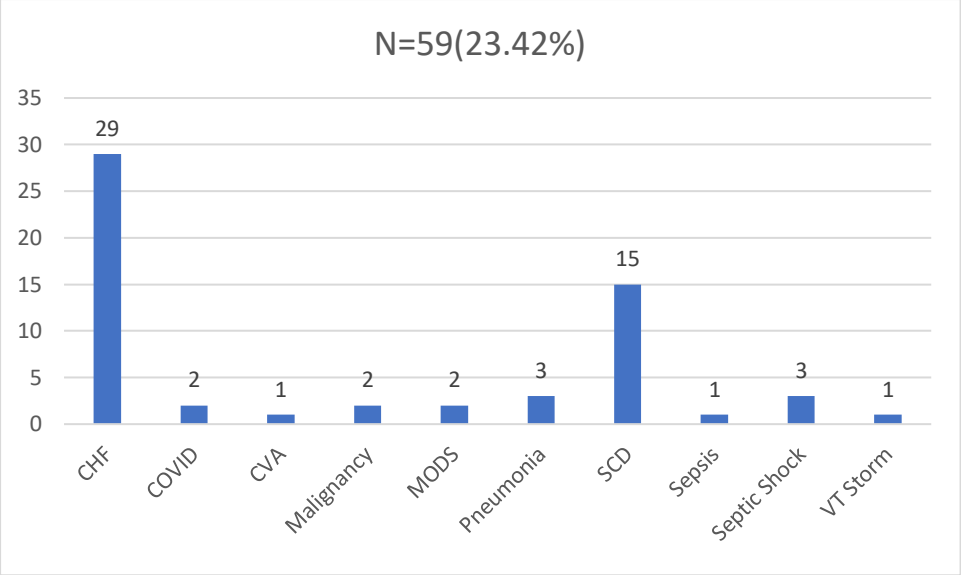

Figure 6: Etiology of mortality

Out of 252 patients, 59(23.41%) patients had died. Cardiovascular cause for mortality was found in 45(17.85%) patients, and non-cardiovascular cause for mortality was found in 14(5.55%) of patients. The main cardiovascular cause of mortality was congestive heart failure found in 29(49.2%) patients, followed by sudden cardiac death in 15(25.4%) patients.

Table 24: Association between Mortality and Parameters

Parameters	Mortality		p-value
	Present (n = 59)	Absent (n = 193)	
Age (Years)	56.54 ± 14.27	55.34 ± 12.53	0.268[1]
Gender			0.345[3]
Male	47 (79.7%)	142 (73.6%)	
Female	12 (20.3%)	51 (26.4%)	
Device Used			0.858[3]
CRT-D	24 (40.7%)	76 (39.4%)	
CRT-P	35 (59.3%)	117 (60.6%)	
Type of Cardiomyopathy			0.055[3]
Ischemic	25 (42.4%)	56 (29.0%)	
Non ischemic	34 (57.6%)	137 (71.0%)	
NYHA Class (Baseline)* **			0.023[3]
II	9 (15.3%)	38 (19.7%)	
III	39 (66.1%)	142 (73.6%)	
IV	11 (18.6%)	13 (6.7%)	
DM (Yes)	39 (66.1%)	104 (53.9%)	0.097[3]
HTN (Yes)	34 (57.6%)	98 (50.8%)	0.357[3]
Dyslipidemia (Yes)* **	34 (57.6%)	81 (42.0%)	0.035[3]
Smoking (Yes)* **	25 (42.4%)	46 (23.8%)	0.006[3]
P/H/O Heart Failure (Yes)* **	39 (66.1%)	65 (33.7%)	<0.001[3]
Atrial Fibrillation (Baseline) (Yes)	6 (10.2%)	12 (6.2%)	0.384[2]
VT/NSVT (Yes)	17 (28.8%)	42 (21.8%)	0.263[3]
CHB (Yes)	14 (23.7%)	40 (20.7%)	0.623[3]
Heart Rate (BPM) (Baseline)* **	72.88 ± 14.25	72.68 ± 8.18	0.035[1]
QRSd (ms) (Baseline)	163.76 ± 24.96	169.28 ± 23.75	0.076[1]
QRSd (Baseline)			0.374[3]
<150 ms	10 (16.9%)	24 (12.4%)	
≥150 ms	49 (83.1%)	169 (87.6%)	
Bundle Branch Block			0.315[2]
Atypical	4 (6.8%)	5 (2.6%)	
Left	51 (86.4%)	176 (91.2%)	
Right	4 (6.8%)	12 (6.2%)	
Baseline QRS Axis			0.645[2]
LAD	52 (89.7%)	179 (92.7%)	
Normal	5 (8.6%)	11 (5.7%)	
RAD	1 (1.7%)	3 (1.6%)	
Prolonged PR (Yes)	17 (38.6%)	61 (36.7%)	0.818[3]
NT-Pro BPN (pg/mL) (Baseline)* **	4059.03 ± 3324.46	2755.09 ± 3068.91	0.006[1]
6MWT (m)	399.40 ± 104.85	347.70 ± 139.91	0.371[4]

Parameters	Mortality		p-value
	Present (n = 59)	Absent (n = 193)	
LVIDd (Baseline)	64.73 ± 10.92	65.90 ± 9.80	0.614[1]
LVIDs (Baseline)	53.73 ± 11.56	54.67 ± 10.29	0.689[1]
LVEF (%) (Baseline)	28.97 ± 8.46	29.62 ± 8.22	0.540[1]
EDV (mL) (Baseline)	183.44 ± 49.71	196.73 ± 71.71	0.494[1]
ESV (mL) (Baseline)	132.18 ± 43.34	141.92 ± 58.44	0.536[1]
SPWD (ms) (Baseline)	173.83 ± 86.50	197.67 ± 90.08	0.220[1]
Q-AE (ms)	161.08 ± 43.08	158.17 ± 35.92	0.824[4]
Q-PE (ms)	108.69 ± 33.94	98.24 ± 26.73	0.316[4]
AE PE Difference (ms)	50.85 ± 18.94	60.91 ± 30.91	0.144[4]
IVS Thickness (mm) (Baseline)	8.70 ± 2.98	8.95 ± 2.54	0.349[1]
Posterior Wall Thickness (mm) (Baseline)	9.74 ± 2.72	10.87 ± 11.53	0.452[1]
MR (Baseline)			0.152[3]
Absent	3 (5.4%)	12 (6.3%)	
Trivial	6 (10.7%)	40 (21.1%)	
Mild	20 (35.7%)	78 (41.1%)	
Moderate	22 (39.3%)	52 (27.4%)	
Severe	5 (8.9%)	8 (4.2%)	
RV Dysfunction (Baseline) (Yes)* **	10 (16.9%)	9 (4.7%)	0.004[2]
Loop Diuretic (Baseline) (Yes)	56 (94.9%)	185 (95.9%)	0.723[2]
MRA (Baseline) (Yes)	54 (91.5%)	172 (89.1%)	0.595[3]
Beta-Blocker (Baseline) (Yes)	52 (88.1%)	179 (92.7%)	0.284[2]
ARB (Baseline) (Yes)	14 (23.7%)	55 (28.5%)	0.472[3]
ARNI (Baseline) (Yes)	2 (3.4%)	6 (3.1%)	1.000[2]
ACE Inhibitor (Baseline) (Yes)	36 (61.0%)	106 (54.9%)	0.409[3]
Digoxin (Yes)	40 (67.8%)	109 (56.5%)	0.122[3]
Amiodarone (Yes)* **	21 (35.6%)	41 (21.2%)	0.025[3]
MRI LV EDV Absolute (mL)	334.67 ± 303.19	235.52 ± 103.56	0.957[1]
MRI LV EDV Normalized (mL)	205.33 ± 194.63	140.21 ± 60.08	0.897[1]
MRI LV ESV Absolute (mL)	282.33 ± 285.08	182.65 ± 97.89	0.872[1]
MRI LV ESV Normalized (mL)	173.67 ± 182.17	108.29 ± 56.68	0.956[1]
MRI LVEF (%)	20.67 ± 8.39	24.09 ± 9.42	0.557[4]
MRI RWMA			0.179[2]
Nil	0 (0.0%)	5 (8.8%)	
Global	2 (66.7%)	45 (78.9%)	
Anterior Wall	0 (0.0%)	6 (10.5%)	
Septum	1 (33.3%)	1 (1.8%)	
PCWP (mmHg)	24.05 ± 7.88	19.76 ± 8.30	0.054[4]
LV EDP (mmHg)* **	25.05 ± 7.98	19.49 ± 6.90	0.008[4]
MAP (mmHg)* **	33.95 ± 9.13	28.42 ± 11.09	0.020[1]
H/O AV Nodal Ablation (Yes)	0 (0.0%)	1 (0.5%)	1.000[2]
QLD Time (ms)	-	145.68 ± 35.96	-
LV Lead Position			0.648[2]
PLV	40 (69.0%)	144 (75.0%)	
Lateral	13 (22.4%)	36 (18.8%)	
Epicardial	4 (6.9%)	8 (4.2%)	
MCV	1 (1.7%)	2 (1.0%)	
Arrythmias (Yes)	5 (8.9%)	16 (8.3%)	1.000[2]
Origin of Arrythmias* **			0.005[2]

Parameters	Mortality		p-value
	Present (n = 59)	Absent (n = 193)	
None	51 (91.1%)	176 (91.7%)	
Supraventricular	1 (1.8%)	15 (7.8%)	
Ventricular	4 (7.1%)	1 (0.5%)	
Biventricular Pacing	96.07 ± 13.88	97.22 ± 8.58	0.504[1]
Response (Present)* **	18 (30.5%)	135 (69.9%)	<0.001[3]

The following parameters were statistically significant:

Table 25: Statistically significant parameters(Mortality present vs. mortality absent)

Variable	Mortality present	Mortality absent	P-value
NYHA Class (Baseline)* **			0.023[3]
II	9 (15.3%)	38 (19.7%)	
III	39 (66.1%)	142 (73.6%)	
IV	11 (18.6%)	13 (6.7%)	
Smoking (Yes)* **	25 (42.4%)	46 (23.8%)	0.006[3]
P/H/O Heart Failure (Yes)* **	39 (66.1%)	65 (33.7%)	<0.001[3]
NT-Pro BPN (pg/mL) (Baseline)* **	4059.03 ± 3324.46	2755.09 ± 3068.91	0.006[1]
RV Dysfunction (Baseline) (Yes)* **	10 (16.9%)	9 (4.7%)	0.004[2]
Amiodarone (Yes)* **	21 (35.6%)	41 (21.2%)	0.025[3]
LV EDP (mmHg)* **	25.05 ± 7.98	19.49 ± 6.90	0.008[4]
MAP (mmHg)* **	33.95 ± 9.13	28.42 ± 11.09	0.020[1]
Presence of Arrhythmias* **			0.005[2]
None	51 (91.1%)	176 (91.7%)	
Supraventricular	1 (1.8%)	15 (7.8%)	
Ventricular	4 (7.1%)	1 (0.5%)	
Response (Present)* **	18 (30.5%)	135 (69.9%)	<0.001[3]

Amongst those groups who had mortality, 66.1% belonged to functional class III, whereas those who did not have mortality had 73.6% patients in NYHA class III (p=0.023). And 18.6% belonged to NYHA class IV who had mortality when compared to 6.7% who did not have mortality (p 0.023). Smoking and past history of heart failure were found in 42.4 and 66.1 % of patients who had mortality, whereas it was 22.8% and 33.7% respectively in patients who did not have mortality (p 0.006). Mean Pro BNP value in patients who had mortality was 4059.03pg/ml, which was higher than those patients who did not have mortality, wherein it was 2755.09pg/ml (p 0.006), the strength of association (Point-Biserial Correlation) = 0.17 (Small Effect Size). Amiodarone usage was found in 35.6% of those who had mortality, which was higher than the group who did not have mortality, wherein it was 21.2% (0.025).

Amongst those who had mortality, RV dysfunction was present in 16.9% when compared to those who did not have mortality, wherein it was 4.7%(p= 0.004).

Amongst those who had mortality, ventricular tachycardia was found in 7.1%, whereas it was 0.5% in those who did not have mortality(p 0.005)

Hemodynamic parameters like left ventricular end-diastolic pressure and mean pulmonary arterial pressure were 25.05 mmHg and 33.95mmHg respectively in patients who had mortality which was higher than those patients who did not have mortality, wherein it was 19.49 mmHg and 28.42 mmHg respectively (p= 0.008 for LVED and 0.020 for mean pulmonary arterial pressure).

The response rate was 30.5% in those who had mortality which was lesser when compared to the group who did not have mortality, wherein it was 69.9% (p=0.001), the strength of association between the two variables (Cramer's V) = 0.34 (Moderate Association). The absence of response was associated with mortality with an odds ratio of 5.3(2.81-9.99) and a relative risk of 3.25(2.17-5.76).

Multivariate analysis of parameters for mortality which were significant on univariate analysis

Table 26: Parameters on multivariate analysis

Variables	Relative risk(95% CI)	P-value
NYHA Class III	0.76(0.48-1.2)	0.257
NYHA Class IV	2.1(1.3-3.5)	0.0024
Smoking	1.87(1.21-2.9)	0.0049
Past History of HF	2.77(1.72-4.4)	<0.0001
RV dysfunction	2.50(1.52-4.1)	0.0003
Use of amiodarone	1.69(1.08-2.65)	0.02
Presence of VT	3.59(2.18-5.9)	0.0001
Presence of response	0.28(0.17-0.46)	0.0001

Multivariate analysis showed the following results: Presence of NYHA class IV at baseline was associated with increased mortality with a relative risk of 2.1(p 0.0024). Presence of smoking (RR 1.87; p 0.049), past history of HF(RR 2.87; p <0.0001), RV dysfunction(RR 2.50; p 0.0003) and presence of ventricular tachycardia(RR 3.59; p 0.0001) at baseline was associated with increased mortality. The use of amiodarone was associated with mortality with an RR of 1.69(p 0.02). The presence of response was associated with reduced mortality with a relative risk of 0.28(p 0.0001).

Following important parameters which were statistically **not** significant:

Table 27: Important statistically nonsignificant parameters(Mortality present vs mortality absent)

Variable	Mortality present	Mortality absent	P-value
Age (Years)	56.54 ± 14.27	55.34 ± 12.53	0.268[1]
Gender			0.345[3]
Male	47 (79.7%)	142 (73.6%)	
Female	12 (20.3%)	51 (26.4%)	
Device Used			0.858[3]
CRT-D	24 (40.7%)	76 (39.4%)	
CRT-P	35 (59.3%)	117 (60.6%)	
Type of Cardiomyopathy			0.055[3]
Ischemic	25 (42.4%)	56 (29.0%)	
Non ischemic	34 (57.6%)	137 (71.0%)	
QRSd (ms) (Baseline)	163.76 ± 24.96	169.28 ± 23.75	0.076[1]
QRSd (Baseline)			0.374[3]

<150 ms	10 (16.9%)	24 (12.4%)	
≥150 ms	49 (83.1%)	169 (87.6%)	
Bundle Branch Block			0.315[2]
Atypical	4 (6.8%)	5 (2.6%)	
Left	51 (86.4%)	176 (91.2%)	
Right	4 (6.8%)	12 (6.2%)	
LVEF (%) (Baseline)	28.97 ± 8.46	29.62 ± 8.22	0.540[1]

The mean age of patients who had mortality was 56.54 years which was higher than those who did not have mortality, wherein it was 55.34 years, although this finding was statistically not significant (p 0.268). Amongst those who had mortality, males were 79%, females were 20.3%, whereas in those who did not have mortality, males were 73% and females 26.4%, the difference was not statistically significant (p 0.345).

CRT-D was implanted in 40.7% and 39.4% in those who had mortality and those who did not have mortality, respectively (p 0.85). And CRT-P was implanted in 59.3% and 60.6% in those who had mortality and those who did not have mortality, respectively (p 0.85).

Ischemic etiology was found in 42.4% and 29.0 % in those who had and those who did not have mortality, respectively. And non-ischemic etiology was found in 57.6% and 71.0% in those who had mortality and those who did not have mortality, respectively, though this difference was statistically not significant (p= 0.055).

The mean QRS duration in those who had mortality was 163.76ms, and in those who did not have mortality was 169.28ms, not significant statistically (p 0.076). Left bundle branch block was found in 86.4% and 91.2% in those who had mortality and those who did not have mortality, respectively (p 0.315).

The mean LV ejection fraction was 28.97% in those who had mortality, and it was 29.62% in those who did not have mortality (p 0.540)

Survival analysis

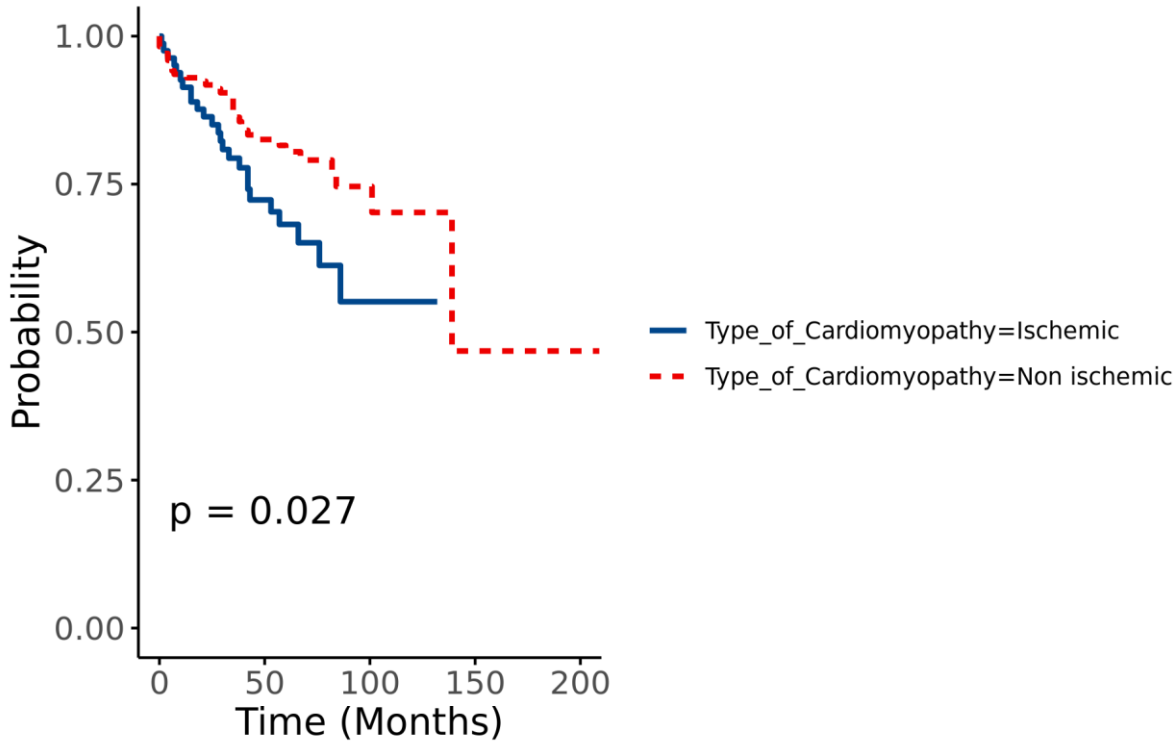

Figure 7: Kaplan mier curve depicting freedom from mortality in groups based on etiology of cardiomyopathy

Patients who had undergone CRT-D/P implantation for nonischemic cardiomyopathy showed better survival when compared to the group who had ischemic cardiomyopathy, with a log-rank p-value of 0.027.

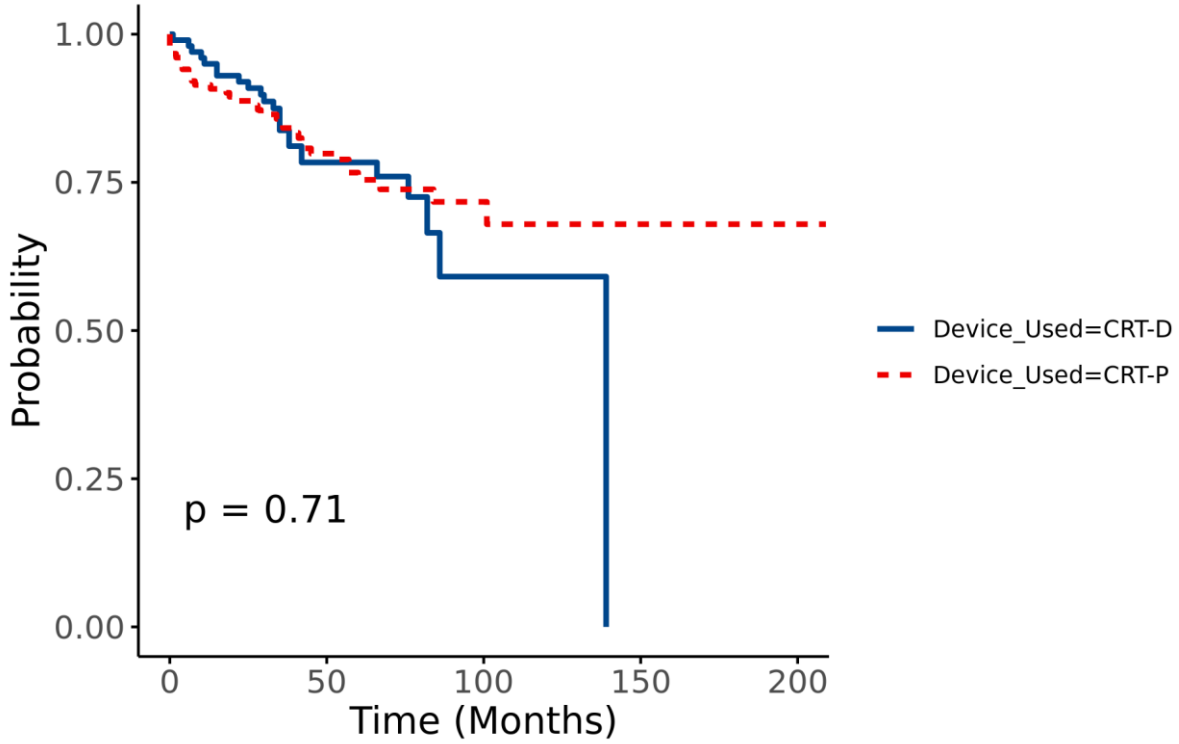

Figure 8: Freedom from mortality in groups based on the type of device used

There was no difference in survival patterns in patients who had undergone CRT-D or CRT P.

Discussion

In this hospital-based retrospective study, 252 patients who had undergone CRT-D/P implantation at our hospital were analyzed. It was carried out to assess the clinical outcomes and elucidate the factors which are associated with response to CRT. All consecutive patients from January 2004 to December 2019 were taken for study. Mean Follow up period being 4.5 ±2.6 years.

Baseline characteristics

Of the total patients analyzed, males (n=189,75%) outnumbered females (n=63,25%) with a ratio of 3:1. The mean age of the study population was 55.11 years ± 12.93 years.

Diabetes mellitus was the most commonly seen comorbidity in the study population with an overall prevalence of 52.3%, followed by hypertension 52.3% and dyslipidemia 45.6%. 41.2% had a history of heart failure. History of ventricular tachycardia in 23.4%, atrial fibrillation in 7.2%, and complete heart block in 21.4%. Naik A et al(10), in their study, had a male population of 79%, a history of VT was found in 24%, and atrial fibrillation in 5.2%. The mean age of their study population was 60.12 years.

CRT-P implantation was done in 60.3%, and CRT-D was implanted in 39.6%. Non-ischemic heart disease as the etiology was seen 67.8% and ischemic etiology in 32.1%. Predominantly patients were in NYHA FC III (71.8%) during device implantation. Bristow et al(8)**,** in the COMPANION trial, had 54% of patients with ischemic etiology, and 87% of patients in their study were in NYHA class III. Naik A et al(10), in their study, had 27% patients with ischemic etiology. Cleland et al(3) in the CARE HF trial had 40% patients with ischemic etiology. Varying percentages of ischemic etiology are probably due to varying demographics in western and our population.

ECG findings

Our study population had a mean QRS duration of 167ms with a standard deviation of ±24ms. 90.07% of patients had left bundle branch block, and right bundle branch block was seen 6.3%. Naik A et al(10), in their study, had a mean QRS duration of 152±32ms, and 69% of patients had LBBB. Bristow et al(8) in the COMPANION trial, had a mean QRS duration of 160ms, left bundle branch block in 73%, and right bundle branch block in 10% of patients. Abraham et al(25), in the MIRACLE study, had a mean QRS duration of 167ms. Our study data is comparable to western data; patients with RBBB also had undergone CRT implantation; as in our study, all consecutive patients with different etiologies were included in contrast to other studies where only ischemic and non-ischemic patients were included.

Echo parameters

The echocardiographic parameters at the baseline showed a mean LV internal diameter during diastole of 65.62mm, LV internal diameter during systole 54.49mm, and mean LV ejection fraction was 29.46%. Bristow et al(8), in the COMPANION trial, had a mean LVEF of 21%, and LV internal diameter during diastole was 67mm. Naik A et al(10), in their study, had a mean LVEF of 24±5%. Abraham et al(25), in the MIRACLE study, had an LVEF of 21.8%. Chung et al(29) in the PROSPECT trial had a mean LVEF of 23.6%. Our study had slightly higher LVEF at baseline, probably due to the inclusion of all those patients who were undergoing up-gradation from pacemakers to CRT.

The mean end-systolic volume in baseline was 193.52ml, end-diastolic volume was 139.58ml. Naik A et al(10), in their study, had an LV EDV of 197±114ml and an LV ESV of 163± 99. The results of our study are consistent with this study.

Markers of dyssynchrony like mean septum to posterior wall delay in our study was 192.98ms, whereas interventricular delay was 58ms. Chung et al(29), in the PROSPECT trial, had studied echo parameters of dyssynchrony with respect to response, although none of the echo parameters predicted response in their study. Cut-offs mentioned in their study for diagnosing dyssynchrony were SPWP >130 and interventricular delay >40ms. In our study, the mean values mentioned above demonstrated dyssynchrony at baseline.

Right ventricular dysfunction was present in 7.53% of patients in our study.

Change in parameters in follow-up.

In our study, over a follow-up period of 4.5±6 years, 59(23.41%) patients had died. 136 54.4% of patients moved from NYHA Class III to NYHA II in follow-up. Cleland et al(3). (3), in the CARE-HF study after a mean follow-up of 18 months, found that the death in the CRT group was 20%. 25.6% of patients were in NYHA class I, 37.7% in NYHA class II, while 19.55% were in NYHA class III.

The mean QRSd (ms) decreased from 167.99 at the baseline to a value of 131.31 at the follow-up. Bleeker et al. (30), in 2007 in their study observed that there was a significant reduction in QRS duration post CRT implantation from 168±27 to 151±25 ms (*P*-value≤0.001). Coppola et al(31) 2016, in their study, found that QRS duration came down from 166 ± 23 ms to 143 ± 20 ms, p-value-<0.001 post CRT implantation. The findings of our study correlate with these findings.

The mean LVEF (%) increased from a minimum of 29.46 at the baseline to a maximum of 37.07 at the follow-up. Zhang et al(32), in 2006, observed that in CRT patients, LVEF

improved from 26.5+9.3% to 34.2+10.5%. The findings of our study are similar to these findings.

The mean ESV (mL) decreased from a maximum of 139.58 at the baseline to a minimum of 125.38 at the follow-up, with a percent change of 30%. Cleland et al(3). (3), in the CARE-HF study, had a reduction in ESV by 26% in follow up which was statistically significant. Cheuk et al. (33) had shown in their study that a reduction in LVESV of 10% signified clinically relevant reverse remodeling, which is a strong predictor of lower long-term mortality and heart failure events.

Predictors of response in CRT

Response to CRT was defined as a change in LVEF >/= to 5% with improvement in NYHA functional class by at least one and non-responders as a change in LVEF < 5% with worsening NVHA functional class or no improvement in NYHA functional class. Responder rates in our study were 60.71%, and non-responders were 39.28%. Chung et al(29) in the PROSPECT trial had a non-responder rate of 31%, Abraham et al(25) in the MIRACLE study had a non-responder rate of 33%. A relatively higher non-responder rate in our study is probably due to the inclusion of all the subsets of the population, like those requiring up-gradation or those with CHB and concurrent LV dysfunction.

The most important predictor of response in our study after multivariate analysis was baseline QRS duration. QRS duration of ≥ 150ms at the baseline predicted response to CRT. Van Bommel et al(34), in their sub-analysis of the prospect trial, also had one of the predictors of response as elevated QRS duration at baseline (p 0.0001). Traditional factors that are associated with the response are mentioned in the figure.

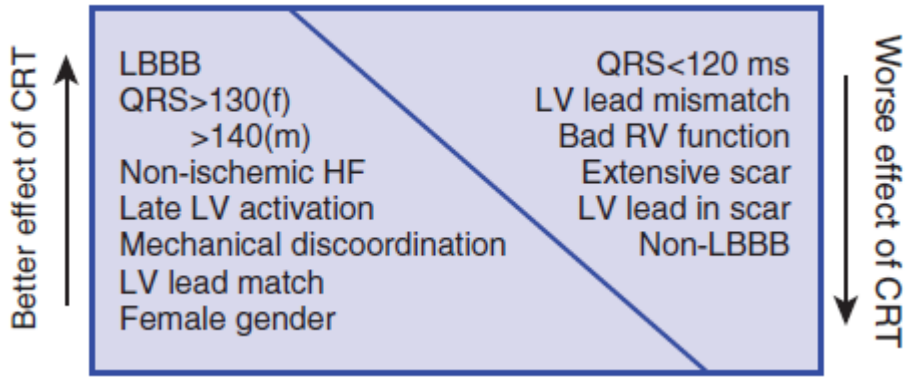

Figure 9: Predictors of response and no response to CRT(12)

However, in our study, except for baseline QRS duration, no other factor predicted response (after multivariate analysis). This can be attributable to a heterogeneous group of patients with different etiologies taken up in our study, which reflects real-world scenarios, unlike in these clinical trials wherein a very selected group of patients are enrolled.

CRT and all-cause mortality

Out of 252 patients, 59(23.41%) patients had died. Cardiovascular cause for mortality was found in 45(17.85%) patients, and non-cardiovascular cause for mortality was found in 14(5.55%) of patients. The main cardiovascular cause of mortality was congestive heart failure found in 29(49.2%) patients, followed by sudden cardiac death in 15(25.4) patients.

Naik A et al(10), in their study, had all-cause mortality of 19.4%. Bristow et al(8), in the COMPANION trial, had all-cause mortality of 25%, 76% of these were due to cardiovascular causes. Van Bommel et al(35), in their study, had a mortality of 20%. Sanjay et al.(36) in Trivandrum heart failure registry reported in-hospital mortality 9.7% and mortality after 3 years, it was 44.8% participants had died. The all-cause mortality rate was lower for participants with HFpEF (40.8%) compared with HFrEF (46.2%; P = .049). In multivariable models, older age (hazard ratio [HR] 1.24 per decade, 95% confidence interval [CI] 1.15-1.33),

New York Heart Association functional class IV symptoms (HR 2.80, 95% CI 1.43-5.48), and higher serum creatinine (HR 1.12 per mg/dL, 95% CI 1.04-1.22) were associated with all-cause mortality. Our study had mortality patterns similar to western and some Indian data, however, high mortality noted in Trivandrum heart failure registry could be due to referral bias, as more sick patients were referred to tertiary care hospital for management.

Multivariate analysis for predicting parameters associated with mortality, we found that the presence of NYHA class IV at baseline was associated with increased mortality with a relative risk of 2.1(p 0.0024). Presence of smoking (RR 1.87; p 0.049), past history of HF (RR 2.87; p <0.0001), RV dysfunction (RR 2.50; p 0.0003), and presence of ventricular tachycardia (RR 3.59; p 0.0001) at baseline was associated with increased mortality. The use of amiodarone was associated with mortality with an RR of 1.69(p 0.02). The presence of response was associated with reduced mortality with a relative risk of 0.28(p 0.0001).

Smoking could be a confounding factor, as it's a risk factor for other diseases like coronary artery disease and malignancies, and hence its presence could increase mortality.

Amiodarone usage was associated with increased mortality, probably due to the overall sick profile of patients using the drug and hence increased risk for mortality.

Other important predictors being the presence of RV dysfunction, ventricular tachycardia, and past history of HF, were associated with increased mortality. Van Bommel et al(35), in their study wherein they, evaluated pre-implantation parameters for predicting morbidity and mortality in HF patients with CRT, found that presence of male gender (HR 1.64, p 0.043), atrial fibrillation (HR 1.18, p 0.001), QRS duration (HR 1.78, p 0.011), 6MWT (HR 1.16, p 0.001), LVESV (HR 0.65, p 0.016), posterolateral lead placement (HR 0.56, p 0.003) predicted all-cause mortality. This is different from our study, probably due to the heterogeneous nature of our study population and longer follow-up (4.5 years vs 6 months).

There was a positive association of presence of response and reduced mortality. We could not find any study comparing the response to mortality.

Survival analysis

Patients who had undergone CRT-D/P implantation for nonischemic cardiomyopathy showed better survival when compared to the group who had ischemic cardiomyopathy, with a log-rank p-value of 0.027. In our study overall survival was better in patients who underwent CRT implantation for nonischemic etiology. In CARE HF trial(3), all cause mortality was similar in ischemic and nonischemic etiology.

Summary and Conclusions

Summary

In this hospital-based retrospective study, 252 patients who had undergone CRT-D/P implantation at our hospital were analysed. It was carried out to assess the clinical outcomes and elucidate the factors which are associated with response to CRT. All consecutive patients from January 2004 to December 2019 were taken for study. Mean Follow up period being 4.5 ±2.6 years.

The findings of our study are summarized below.

1. Patients in the CRT-D group were relatively elder, with a mean age of 58.52 years when compared to patients in the CRT-P group, where the mean age was 53.72 years($p=0.003$).
2. The type of device implanted in males and females was significantly different, as more CRT-D devices being implanted in males (87%) as compared to females (13%), whereas CRT -P was implanted in 67.1% of males and 32.9% in females($p=0.001$).
3. The proportion of comorbidities was more in the CRT-D group, like DM(68%), hypertension (66%), dyslipidemia(58%), smoking(39%) when compared with patients in the CRT-P group(DM 49%, hypertension 43%, Dyslipidemia 37%, smoking 21%).
4. Ischemic etiology of cardiomyopathy was seen in 53% of patients in the CRT-D group, whereas it was 18.4% in the CRT-P group. The proportion of nonischemic etiology was more in the CRT-P group, 81.6%, whereas it was 47% in the CRT-D group($p<0.001$).
5. LVEF on MRI was found to be 19.73% in the CRT-D group of patients, whereas it was 26.47% in the CRT-P group (0.004).
6. All-cause mortality was found in 24%, and 23% in CRT-D and CRT-P groups of patients, respectively, which was similar in both the groups and it was not statistically significant.

7. The mean QRSd (ms) decreased from 167.99 at the baseline to a value of 131.31 at the follow-up.
8. The most important predictor of response in our study after multivariate analysis was baseline QRS duration. QRS duration of ≥ 150ms at the baseline predicted response to CRT.
9. Patients who had undergone CRT-D/P implantation for nonischemic cardiomyopathy showed better survival when compared to the group who had ischemic cardiomyopathy, with a log-rank p-value of 0.027
10. Out of 252 patients, 59(23.41%) patients had died. Cardiovascular cause for mortality was found in 45(17.85%) patients, and non-cardiovascular cause for mortality was found in 14(5.55%) of patients. The main cardiovascular cause of mortality was congestive heart failure found in 29(49.2%) patients, followed by sudden cardiac death in 15(25.4%) patients.
11. Presence of NYHA class IV, smoking, past history of HF, presence of VT, and RV dysfunction predicted mortality. Also, the presence of response was associated with reduced all-cause mortality with a relative risk of 0.28 (p 0.0001).

Limitations

1. This study was a hospital-based study restricted to a single teaching hospital.
2. Out of hospital death inquiry was based on telephonic conversation
3. It's a retrospective study

Conclusions

1. The response rate, mortality, and predictors of response in our study are comparable with the western data.
2. QRS duration at baseline predicted response to CRT.
3. Patients with nonischaemic cardiomyopathy who underwent CRT implantation are associated with better survival.
4. There is a positive association of presence of response to CRT and reduced mortality.

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APPENDIX

grammarly Report: CRT Thesis

Clinical outcomes after cardiac resynchronization therapy: A single center experience

General metrics

93,554	14,181	1523	56 min 43 sec	1 hr 49 min
characters	words	sentences	reading time	speaking time

Score

94

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

Writing Issues

329 Issues left

Critical

329 Advanced

Plagiarism

5 %

8 sources

5% of your text matches 8 sources on the web or in archives of academic publications

Report was generated on Wednesday, Aug 4, 2021, 12:42 PM

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CONSENT FORM

Title of the study: LONG TERM FOLLOW UP OF PATIENTS WITH CARDIAC RESYNCHRONIZATION THERAPY

Participant's name:

Age (in years):

I_____, son/daughter/husband/wife/---------- of _____ declare that (Please tick boxes)

• I have read the above information provide 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 Published[ ]
• I voluntarily agree to take part in this 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 received a copy of this signed consent form [ ]

Name:
Signature:
Name of witness:
Signature:
Relation to participant:

സമ്മതപത്രം

പഠനശീർഷകം. ഹൃദയ പുനരുജ്ജീവനം ചികിത്സ കഴിഞ്ഞ രോഗികളുടെ ദീർഘകാല തുടർചികിത്സ.

രോഗിയുടെ പേര്

വയസ്സ് (വർഷത്തിൽ)

ഞാൻ.....പുത്രൻ/പുത്രി/ദർത്താവ്/ഭാര്യ ..... പ്രസ്താവിക്കുന്നതെന്തെന്നാൽ (ദയവായി കോളങ്ങളിൽ ശരിയടയാളപ്പെടുത്തുക)

മുകളിൽ പറഞ്ഞ ഹൃദയ പുനരുജ്ജീവനം ചികിത്സ കഴിഞ്ഞ രോഗികളുടെ ദീർഘകാല തുടർചികിത്സ എന്ന പഠന സംബന്ധിയായി എനിക്കു നൽകിയ വിവരങ്ങൾ വായിച്ചു എന്നു പ്രസ്താവിക്കുന്നു [ ]

- എന്റെ എല്ലാ സംശയങ്ങളും പരിഹരിച്ചു [ ]
- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം പൂർണ്ണമായും സ്വമേധയാ ആണെന്നും അനുവാദം എനിക്ക് ഏതുസമയത്തും എന്റെ ചികിത്സയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ പിൻവലിക്കാൻ അവകാശമുണ്ടെന്നും ഞാൻ മനസ്സിലാക്കുന്നു [ ]
- ഞാൻ ഈ പഠനത്തിൽ നിന്നും പിൻമാറിയാലും പഠനം നടത്തുന്നവർക്കും സ്ഥാപനത്തിലെ നൈതിക കമ്മിറ്റി അംഗങ്ങൾക്കും എന്റെ ആരോഗ്യരേഖകൾ പരിശോധിക്കുന്നതിന് എന്റെ അനുവാദം ആവശ്യമില്ലെന്ന്ഞാൻ മനസ്സിലാക്കുന്നു. അതിനോട് ഞാൻ യോജിക്കുന്നു [ ]
- എന്നെ തിരിച്ചറിയാനുതകുന്ന വിവരങ്ങൾ ഒന്നും മൂന്നാം കക്ഷികൾക്കു നൽകുകയോ പ്രസിദ്ധീകരിക്കുകയോ ചെയ്യില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു [ ]
- പഠനത്തെപ്പറ്റിയോ പങ്കാളികളുടെ അവകാശങ്ങളെപ്പറ്റിയോ കൂടുതലറിയണമെങ്കിൽ ബന്ധപ്പെടാൻ എനിക്ക് പ്രധാനഗവേഷകനെ ബന്ധപ്പെടാനുള്ള നമ്പർ നൽകിയിട്ടുണ്ട് [ ]
- ഞാൻ സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിക്കുന്നു [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു കോപ്പി എനിക്കു കിട്ടി [ ]

പങ്കെടുക്കുന്നയാളുടെ പേര്

ഒപ്പ്

തീയതി

സാക്ഷിയുടെ പേര്

ഒപ്പ്

പങ്കെടുക്കുന്ന ആളുമായുള്ള ബന്ധം

തീയതി

(സമ്മതം വാങ്ങുന്നയാൾ)

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണപദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ

ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രം വാങ്ങുന്ന ആളുടെ പേര്

ഒപ്പ്

പ്രധാന ഗവേഷകൻ

PATIENT INFORMATION FORM

"LONG TERM FOLLOW UP OF PATIENTS WITH CARDIAC RESYNCHRONIZATION THERAPY"

Name of the Investigators:
Dr. Syed Nawaz Afzal, Dr. Narayanan Namboodri K.K, Dr. Ajit Kumar V. K.

You are being requested to participate in this study to assess the long term follow up of patients with Cardiac Resynchronization Therapy.

This is a Retrospective and Prospective observational study to understand the Long term outcomes in patients who undergo Cardiac Resynchronization Therapy(CRT).

Our study aims to assess the long term outcomes and elucidate factors associated with CRT response.

Who will be included in this study?
All patients who underwent CRT implantation in SCTIMST until 31/12/2018.

If you take part what will you have to do?
After you have consented to be part of the study, you will be interviewed for your disease status and hospital records will be reviewed for by clinical history and investigations.

Who will undergo CRT?
Patients with Heart Failure with reduced EF and evidence of dyssynchrony

Can you withdraw from this study after it starts?
Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

Whether there is any risk related to this study?
There is no individual risk or benefit to the patient himself as it is an observational study. Rarely if any harm happen to patients, they will be managed but no monetary benefits will be provided.

Will your personal details be kept confidential?
The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If at any time you experience any problems, or if you have any further questions, please ask Dr. Syed Nawaz Afzal, Mobile 9557970667, email-afzalkhatib@gmail.com

രോഗിക്കുള്ള കാര്യവിവരണ പത്രം

പഠനശീർഷകം. ഹൃദയ പുനരുജ്ജീവനം ചികിത്സ കഴിഞ്ഞ രോഗികളുടെ ദീർഘകാല തുടർചികിത്സ

ഗവേഷകരുടെ പേര്

ഡോ. സെയ്ദ് നവാസ് അഫ്സൽ,
ഡോ. നാരായണൻ നമ്പൂതിരി കെ കെ,
ഡോ. അജിത്കുമാർ വി കെ.

ഹൃദയ പുനരുജ്ജീവനം ചികിത്സ കഴിഞ്ഞ രോഗികളുടെ ദീർഘകാല തുടർചികിത്സയുടെ നേട്ടം വിലയിരുത്തുന്ന പഠനത്തിൽ പങ്കെടുക്കാൻ ഞങ്ങൾ താങ്കളോട് അഭ്യർത്ഥിക്കുന്നു.

ഹൃദയ പുനരുജ്ജീവനം ചികിത്സ (സിആർടി) നടത്തിയ രോഗികളുടെ ദീർഘകാലത്തെ നേട്ടം മനസ്സിലാക്കാൻ നടത്തുന്ന ഒരു ഭൂതകാല - ഭാവികാല നിരീക്ഷണ പഠനമാണ്.

സിആർടി പ്രതികരണങ്ങളുടെ ദീർഘകാല നേട്ടങ്ങളും വിലയിരുത്തുക സ്വഭാവപ്പെട്ട ഘടകങ്ങളും വിശദീകരിക്കുക എന്നിവയും നമ്മുടെ പഠനം ലക്ഷ്യമാക്കുന്നു.

ഈ പഠനത്തിൽ ആരെയൊക്കെ ഉൾപ്പെടുത്തും?
31/12/2018 വരെ SCTIMST യിൽ സിആർടി സ്ഥാപിച്ച എല്ലാ രോഗികളെയും പഠനത്തിൽ ഉൾപ്പെടുത്തും.

പഠനത്തിൽ പങ്കെടുക്കുകയാണെങ്കിൽ താങ്കളെന്തു ചെയ്യണം?
താങ്കൾ പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിച്ചശേഷം താങ്കളുടെ രോഗ അവസ്ഥസംബന്ധിച്ച് ഒരഭിമുഖം നടത്തുകയും ചികിത്സാചരിത്രവും പരിശോധനാവിവരങ്ങളും വിലയിരുത്തുകയും ചെയ്യും.

ആരാണ് സിആർടിക്ക് വിധേയരാകുന്നത്?

ഹൃദയപരിക്ഷീണനയും രക്തത്തിന്റെ ഇടതു വെൻട്രിക്കിളിൽനിന്നുള്ള പുറന്തള്ളൽ മൂല്യവും കുറഞ്ഞ ഏകകാലികമായ ഹൃദയപ്രവർത്തനമില്ലായ്മയുടെ ലക്ഷണമുള്ള രോഗികൾ.

പഠനമാരംഭിച്ചശേഷം താങ്കൾക്ക് പഠനത്തിൽ നിന്നും പിൻമാറാനാകുമോ?
താങ്കളുടെ പഠനത്തിലെ പങ്കാളിത്തം സ്വമേധയും പഠനത്തിൽ നിന്നും ഏതു സമയവും പിൻമാറാൻ സ്വാതന്ത്ര്യവുമുള്ളതാണ്. താങ്കളങ്ങിനെ ചെയ്യുന്നതുകൊണ്ട് ഈ ആശുപത്രിയിലെ താങ്കളുടെ ചികിത്സയെ ഒരുവിധത്തിലും ബാധിക്കില്ല.

ഈ പഠനവുമായി ബന്ധപ്പെട്ട് എന്തെങ്കിലും അപകടമുണ്ടോ?
ഇത് ഒരു നിരീക്ഷണ പഠനമാകയാൽ വ്യക്തിപരമായ അപകടമോ നേട്ടങ്ങളോ രോഗിക്കുണ്ടാകില്ല. രോഗിക്ക് എന്തെങ്കിലും അപായം അപൂർവ്വമായി സംഭവിച്ചാൽ അത് കൈകാര്യം ചെയ്യും, സാമ്പത്തിക സഹായം നൽകാനാവില്ല.

താങ്കളുടെ വ്യക്തി വിവരങ്ങൾ രഹസ്യമായി സൂക്ഷിക്കുമോ?

പഠനഫലങ്ങൾ വൈദ്യശാസ്ത്ര ജേർണലിൽ പ്രസിദ്ധീകരിച്ചേക്കാമെങ്കിലും താങ്കളെ പേരുകൊണ്ടോ മറ്റുവിധത്തിലോ തിരിച്ചറിയാനിടയാക്കുന്നതൊന്നും പ്രസിദ്ധീകരണത്തിലോ പ്രദർശനങ്ങളിലോ ഒരിടത്തും ഉണ്ടാകില്ല. താങ്കൾ പഠനത്തിൽ പങ്കെടുക്കുകയാണെങ്കിൽ, താങ്കളുടെ പ്രത്യേക അനുവാദമില്ലാതെ ക്ലിനിക്കൽ വിശദാംശങ്ങൾ പഠനവുമായി ബന്ധപ്പെട്ട ആളുകൾ പരിശോധിച്ചേക്കാം.

താങ്കൾക്ക് കൂടുതൽ ചോദ്യങ്ങളുണ്ടെങ്കിൽ ദയവായി ബന്ധപ്പെടുക

ഡോ. സെയ്ദ് നവാസ് അഫ്സൽ, (പ്രധാന ഗവേഷകൻ) സീനിയർ റെസിഡന്റ്,

ഫോൺ 9557970667 ഇമെയിൽ: afzalkhatib@gmail.com

പഠനത്തിന്റെ നൈതീക അനുവാദസംബന്ധമായ വിശദീകരണത്തിന് താങ്കൾക്ക് ബന്ധപ്പെടാം.

മെമ്പർസെക്രട്ടറി **SCTIMST-IEC**

ഫോൺ 0471-2524234 ഇമെയിൽ: **iec.mem.sec@sctimst.ac.in**

PROFORMA

Name - Age - Sex –
Weight - Height –
Hopsital No. –

Chief complaints : - i) Angina – effort angina/rest angina
ii) SOB
iii) Palpitation
iv) Syncope
v) Pedal swelling
vi) Others –

PAST H/O MI –

Risk factors – DM/HTN/DLP/SMOKER/THYROID DISEASE/ PERIPHERAL/ARTERIAL DISEASE

Current Medications –

Classification – NYHA CLASS

Clinical Examination
PR = , Distal pulses palpable Y/N
BP =
JVP - Pedal Edema -
Cardiovascular examination –
Chest –
Any other relevant findings –

Investigations
ECG
PRE CRT
POST CRT
OFF CRT

X- Ray –

2D ECHO - LV dimensions
Ejection fraction
LVESV
LVEDV

TROP T –

PRO BNP –

S. CREATININE –

FASTING LIPID PROFILE –
THYROID PROFILE –
ESR –

CARDIAC CATH STUDY REPORT

CARDIAC MRI REPORT

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)
Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1491 /NOVEMBER-2019 07.11.2019

Dr. Syed Nawaz Afzal
Senior Resident
Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Syed Nawaz Afzal,

Thank you for submitting documents related to your proposal titled "LONG TERM FOLLOW UP OF PATIENTS WTH CARDIAC RESYNCHRONIZATION THERAPY (IEC/ 1491)" to the IEC for review.

List of documents:

1. Covering Letter addressed to the Charperson, IEC, SCTIMST date 10.09.2019 with checklist
2. TAC Approval Letter
3. IEC Application Form
4. Forwarding Letter from the HOD
5. Project Proposal
6. Patient Information Sheet and Consent Form in English and Malayalam
7. Proforma
8. CV of Principal Investigator and Co-Principal Investigators

IEC Recommendations

1. Remove the name of the patient from the proforma. Use a unique identifier.
2. In the proforma collect information about the other parameters – the timing should be specified- during follow up, or at discharge or both.
3. Attach a telephone script for inviting the patients for the review (in English and Malayalam)

One set of all the documents including those revised may be submitted. The covering letter should indicate the revisions made.

Sincerely,

Mala Ramanathan
Member Secretary, IEC