CLINICAL AND CARDIAC MAGNETIC RESONANCE (CMR) FEATURES IN HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFpEF)

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DM (Cardiology) Thesis

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DEPARTMENT OF CARDIOLOGY

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

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Clinical and cardiac magnetic resonance (CMR) features in heart failure with preserved ejection fraction (HFpEF)

A THESIS SUBMITTED BY

Dr Sudipta Mondal

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM

In partial fulfillment of the requirements for the award of

DM (CARDIOLOGY)

2023

Declaration by the student

CERTIFICATE

I, Dr Sudipta Mondal, hereby certify that I have personally carried out the work in the thesis titled **Clinical and cardiac magnetic resonance (CMR) features in heart failure with preserved ejection fraction (HFpEF),** in the Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum.

I further declare that before this date, no part of this thesis has been submitted for the award of any other degree or diploma.

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The thesis titled **Clinical and cardiac magnetic resonance (CMR) features in heart failure with preserved ejection fraction (HFpEF),** was carried out under my direct guidance and supervision, and no part of this thesis was submitted for awarding any degree or diploma, before this date.

Clearance from the Institutional Ethics Committee was obtained for conducting this study.

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APPROVAL OF THE THESIS

The thesis titled

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Signature of the guide.

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Dr Sudipta Mondal

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List of Abbreviations

1.	ACC	American College of Cardiology
2.	ACEi	Angiotensin converting enzyme inhibitor
3.	AF	Atrial fibrillation
4.	AHA	American Heart Association
5.	ARB	Angiotensin receptor blocker
6.	BNP	B-type natriuretic peptide
7.	CA	Cardiac amyloidosis
8.	CMR	Cardiac magnetic resonance
9.	CS	Cardiac sarcoidosis
10.	DCM	Dilated cardiomyopathy
11.	ECV	Extracellular volume
12.	EF	Ejection fraction
13.	ESC	European Society of Cardiology
14.	HCM	Hypertrophic cardiomyopathy
15.	HF	Heart failure
16.	HFA	Heart Failure Association
17.	HFimpEF	HF with improved EF
18.	HFmrEF	HF with mildly reduced EF
19.	HFpEF	HF with preserved ejection fraction
20.	HFrEF	HF with reduced ejection fraction
21.	HOCM	Hypertrophic obstructive cardiomyopathy
22.	HRS	Heart Rhythm Society
23.	ICM	Ischemic cardiomyopathy
24.	JMHW	Japanese Ministry of Health and Welfare
25.	LGE	Late gadolinium enhancement
26.	NT-proBNP	N-terminal pro-B-type natriuretic peptide
27.	SGLT2i	Sodium Glucose Transporter 2 inhibitor
28.	SPECT	Single-photon emission computed tomography
29.	THFR	Trivandrum Heart Failure Registry
30.	VT	Ventricular tachycardia

Synopsis of the study

Aims and objective: Myocardial fibrosis has been implicated in pathophysiology of HFpEF in recent past. This study was conceived to document patient characteristics, including demographic profile and to evaluate the presence, and prognostic significance, of myocardial fibrosis in subjects with and without HFpEF, using Cardiac MRI.

Methods: This was a hospital based, ambi-directional, record review study, spread over January 2018 to December 2022 [mean follow up: 25months, IQR 11-44months] selecting HFpEF patients as per existing ASE/ESC guidelines. An age and sex matched control arm was included with 30 consecutive patients without HF. Late gadolinium enhanced (LGE) imaging and T1 mapping were used to assess fibrosis.

Results: Diabetes, hypertension, and obesity ($p < 0.001$) emerged as the strongest risk factors for HFpEF. Left ventricle mass index and left atrium volume index were significantly higher in HFpEF group compared to control ($p < 0.001$). LGE (27% vs 0%, *p = 0.005*) and mid segment (mean ± SD; 1062 ± 64 vs 1020 ± 8, $p < 0.001$) or total average (mean ± SD; 1057 ± 70 vs 1020 ± 4 , $p = 0.006$) T1 value were significantly higher in HFpEF group compared to control group. However there was no significant difference in T2 value ($p = 0.657$).

53.3% of our patients with HFpEF had a clinical event (HF hospitalization or all-cause mortality) during the period of follow up. It was found that average mid-segment (mean ± SD; 1099 ± 67 vs 1019 ± 17, *p < 0.001*) and total average (mean ± SD; 1101 ± 70vs 1007 ± 15, *p < 0.001*) T1 values were significantly higher in event group compared to no-event. There were no difference in LGE prevalence between event and no-event groups. However LGE negative cases had significantly increased T1 values in all segments compared to healthy control group (Total T1, mean ± SD; 1053 ± 62vs 1020 ± 4, *p < 0.*001). Moreover event group was more associated with increased NT Pro-BNP levels ($p = 0.047$), higher loop diuretic dose requirement ($p = 0.005$),

higher carinal angle and cardiomegaly in chest x-ray ($p < 0.001$) and presence of pericardial effusion ($p < 0.001$).

Conclusions

Higher T1 but not T2 was associated with HFpEF group compared to age and sex matched control group. Focal fibrosis as evident by LGE is significantly more in HFpEF. Among HFpEF patients, high T1 myocardial values were associated with a higher rate of all-cause death, stroke and HF hospitalization in short term follow up.

Introduction

Introduction

Heart failure (HF) is defined as a complex clinical syndrome caused by functional and/or structural cardiac abnormalities.(Ponikowski et al., 2016; Yancy et al., 2013) These abnormalities stem from disease or dysfunction of the myocardium, valves, pericardium, endocardium, or the cardiac conduction system and can cause HF. Population studies have estimated an increase in the prevalence of HF of 46% from 2012 to 2030, and a corresponding increase in the cost of HF treatment to $69.8 billion by 2030 in the USA has been forecasted.(Virani et al., 2020) A clear and accurate understanding of the underlying etiology of HF is crucial to the appropriate treatment and subsequent outcome in patients of HF. (Ziaeian and Fonarow, 2016)

While clinical assessment and bedside evaluation continue to remain our fundamental pillars of diagnosis, there has been an unprecedented development in the investigational armamentarium Diagnostic imaging has been the major revolution in medicine in recent years. In fact, medical imaging has been hailed as one of the 10 most important medical advances in the last 1000 years.(*New England Journal of Medicine*, 2000) This development has been most spectacular in the domains of Neurology and Cardiology.

The major advancements in cardiac diagnostic imaging began to take shape with echocardiography. (Edler and Hertz, 2004; Effert et al., 1957) This single technology revolutionized and "democratized" cardiac diagnosis and was followed by subsequent developments in the form of nuclear medicine techniques, (Lebowitz et al., 1975; Pohost et al., 1977) cardiac magnetic resonance imaging (CMRI), (Canby et al., 1987; Ratner et al., 1985) and computed tomography (CT). (Abdulla et al., 2007; Gopalakrishnan et al., 2008)

Today, the availability of such advanced technology has spilled over from high end teaching and research institutions to the domain of routine clinical evaluation and disease management. In the diagnostic work-up of HF patients, and the assessment of their prognosis, cardiac magnetic resonance (CMR) has emerged as a useful non-invasive tool. Compared to the more commonly available echocardiography, CMR has established its superiority in the assessment of left ventricular (LV) volumes and function and in the analysis of wall motion abnormalities and myocardial tissue characteristics. Myocardial fibrosis is a common pathologic manifestation in

heart failure, and the pattern of fibrosis serves as a surrogate marker of the etiology.(Bing and Dweck, 2019) Late gadolinium enhancement (LGE) in CMR enables non-invasive quantification of myocardial fibrosis and is one of the most widely used CMR techniques in identifying etiology and assessing prognosis in patients with HF. Moreover, CMR can identify intracellular abnormalities, myocardial edema, and deposition of extracellular proteins, all of which are important in the pathogenesis of HF. Myocardial tissue characterization parameters (T1, T2, T2*, and extracellular volume (ECV)) can quantify tissue alterations in patients with HF; these include intracellular changes of cardiomyocyte (fat deposition or iron overload), extracellular changes in the myocardial interstitium (e.g., fibrosis or deposition of amyloid proteins), or both (myocardial infarction and/or edema). (Lota et al., 2017; Messroghli et al., 2017; Moon et al., 2013; Patel et al., 2013; Robinson et al., 2019) The classical T1 image reflects the changes in myocardium involving the myocytes and the interstitium. Myocardial interstitial expansion by fibrosis, fluid, or other protein deposits is reflected in the ECV, calculated by T1 pre and post administration of gadolinium and hematocrit.(Moon et al., 2013) For patients who cannot receive gadolinium contrast due to severe renal dysfunction, native T1 acts as a non-exogenous contrast-based endogenous tissue characterization parameter. T2 mapping is sensitive to myocardial edema. Furthermore, T2* is a useful tool to assess tissue iron deposition.(Lota et al., 2017) Several international heart failure guidelines have incorporated CMR imaging in HF; CMR has been shown to change overall patient management in up to 65% of patients with heart failure. (Patel et al., 2013) Taking an extra step forward, the European Association for Cardiovascular Imaging has recommended parametric mapping in the diagnostic evaluation of patients with HF. (Messroghli et al., 2017)

CMR imaging in HF spans the entire spectrum of cardiac etiologies which are associated with deranged cardiac function. Coronary artery disease is the most common and a potentially treatable cause of HF and needs to be assessed in every patient with a new diagnosis of HF. Ischemic cardiomyopathy (ICM) manifests as LGE and usually occurs in the subendocardial to transmural involvement corresponding to a coronary artery distribution. (Adam et al., 2017; Mahrholdt et al., 2005) In addition to LGE, where the pattern of fibrosis can detect scar due to MI, there is growing evidence that stress perfusion CMR is efficacious in identifying myocardial ischemia. The Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery Disease Trial (MR-IMPACT) I, MR-IMPACT II, and Clinical Evaluation of Magnetic

Resonance Imaging in Coronary Heart Disease (CE-MARC) studies have highlighted the equality or superiority of stress perfusion CMR for the detection of CAD when compared to single-photon emission computed tomography (SPECT). (Greenwood et al., 2012; Schwitter et al., 2008, 2013)

Dilated cardiomyopathy (DCM) is a common etiology of heart failure and CMR has emerged as a major diagnostic and prognostic tool in the non-invasive assessment of DCM. LGE was detected in approximately 30–40% of patients with DCM, with the common pattern being mid-wall septal LGE. (Halliday et al., 2017, 2019; McCrohon et al., 2003) Prognostic assessment in patients with non-ischemic cardiomyopathy is also feasible with CMR. (Amzulescu et al., 2015; Becker et al., 2018; Disertori et al., 2016; Puntmann et al., 2016; Sree Raman et al., 2019) A study including 472 patients with DCM found that mid-wall fibrosis was an independent predictor for all-cause mortality after adjustment for LVEF and other clinical factors such as heart rate and blood pressure. (Gulati et al., 2013) Moreover, mid-wall LGE in patients at first diagnosis of DCM was independently associated with subsequent adverse cardiac events and HF rehospitalization. (Sree Raman et al., 2019) Fibrosis/scar has been traditionally considered as a fertile substrate for ventricular arrhythmia and the subsequent risk of SCD; accordingly, CMR is able to identify patients at high risk of SCD. (Chan et al., 2014; Di Marco et al., 2017; Klem et al., 2012)

Hypertrophic cardiomyopathy is also a risk factor for HF. The majority of patients with hypertrophic cardiomyopathy (HOCMobstruction) present as HF with preserved ejection fraction (HFpEF), while only a minority of patients with HCM develop reduced ejection fraction (HFrEF) at a later stage.(Seferović et al., 2019) Fibrosis progression detected by LGE-CMR was associated with LV thinning, increased LV end-diastolic volume, reduced LVEF, and adverse clinical outcomes.(Raman et al., 2019) Those with worsening cardiac function had evidence of higher progression of LGE.(Todiere et al., 2012)

Cardiac amyloidosis (CA) deserves consideration in patients with HFpEF,(Manolis et al., 2019) and early recognition coupled with early treatment has the potential to positively impact prognosis. Ventricular hypertrophy is characteristic of CA, and the most common LGE pattern is global, transmural or subendocardial enhancement, with high native T1 and ECV.(Baggiano et al., 2020; Fontana et al., 2015; Martinez-Naharro et al., 2019; Syed et al., 2010) Apart from LV

hypertrophy, atrial dilation, thickening of the atrial septum, and pericardial effusion are other common morphological features of CA. CMR is known for its superior ability to identify tissue characteristics. As a result, CMR has become an important tool in the diagnosis and assessment of amyloidosis involving the heart.(Baggiano et al., 2020; Brownrigg et al., 2019; Chacko et al., 2019; Syed et al., 2010) LGE improves the diagnosis of CA, but LGE may not detect CA patients in the early phase.(Fontana et al., 2015) in contrast, T1 mapping and ECV have been widely demonstrated to improve the diagnosis in patients with suspected CA.(Baggiano et al., 2020; Banypersad et al., 2015; Martinez-Naharro et al., 2017)

Acute myocarditis can present as new-onset HF, while partial resolution of acute myocarditis can serve as the substrate for DCM. CMR has emerged as a preferred imaging mode for the diagnosis and evaluation of patients with myocarditis. This is attributable to the role of CMR in not only assessing ventricular morphology and function, but also determining the tissue characteristics such as edema and/or fibrosis. The Lake Louise criteria to diagnose myocarditis were formulated in 2009, where myocarditis can be diagnosed if two out of three CMR criteria are positive: edema (increased T2-weighted signal), hyperemia (early gadolinium enhancement), and necrosis (LGE).(Friedrich et al., 2009) LGE pattern is commonly subepicardial and/or mid-wall but can also involve the endocardium.

The clinical features of **cardiac sarcoidosis (CS)** include conduction block, ventricular arrhythmias, and heart failure; although some patients may be asymptomatic.(Kusano and Satomi, 2016) CMR has been proved to be useful in the diagnosis of CS. International guidelines like the updated Japanese Ministry of Health and Welfare (JMHW) criteria and the Heart Rhythm Society (HRS) Expert Consensus Statement mention LGE on CMRI as one of the diagnostic criteria for CS.(Birnie et al., 2014; Terasaki and Yoshinaga, 2017) The pattern of LGE in patients with CS has been variable. Subepicardial, transmural, subendocardial, and mid-wall patterns have all been identified, often involving more than one segment. The basal and/or mid-ventricular septum are the two most common locations of pathological involvement.(Patel et al., 2009; Smedema et al., 2005; Watanabe et al., 2013) In addition to LV LGE, decreased right ventricular ejection fraction (RVEF) and the presence of RV-LGE on CMR have been shown to be associated with an increased risk of adverse outcomes.(Kagioka et al., 2020; Smedema et al., 2017)

Atrial fibrillation (AF) and HF often coexist with an increased mortality risk. Studies showed that AF ablation, when compared to pharmacotherapy, have been associated with reduced all-cause mortality and HF hospitalizations.(Marrouche et al., 2018; Turagam et al., 2019) Left atrial (LA) fibrosis is an important pathological change in the development of AF. This has been reflected in the finding that the extent of atrial fibrosis assessed by LGE-CMR increased the likelihood of recurrent AF.(Marrouche et al., 2018) Apart from LA fibrosis, LV fibrosis has been proposed to be an independent predictor of AF recurrence.(Begg et al., 2020; Neilan et al., 2014)

Ventricular tachyarrhythmias are common in patients with HF. It is now well established that ICD implantation is an effective avenue to prevent SCD in patients with HF. Moreover, catheter ablation has been successfully associated with the prevention of recurrent ventricular tachycardia (VT). Studies from across the world have demonstrated that CMR is useful in guiding VT ablation by localizing potential and actual VT substrates.(Andreu et al., 2014; Dukkipati and Sanz, 2014; Piers et al., 2014)

Clearly, CMR can assess cardiac structure and function accurately and reproducibly. As a consequence, it has evolved into a major non-invasive imaging tool to guide the diagnosis, risk stratification, and management for patients with HF. Its ability to characterize myocardial tissue can help determine the underlying etiology of HF. As more evidence and more outcome data accumulate, CMR will play a greater role in the field of HF in the near as well as distant future. Till date, data on CMR in HFpEF is sparse from our subcontinent. This study titled **Clinical and Cardiac Magnetic Resonance (CMR) features in Heart Failure with preserved ejection fraction (HFpEF)** was designed to establish the CMR characteristics of HFpEF in an Indian cohort.

Review of literature

Review of literature

Definition of Heart Failure

Heart failure is a clinical syndrome manifested by several cardinal symptoms (e.g. breathlessness, fatigue, and ankle swelling) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and peripheral edema). This clinical presentation stems from a structural and/or functional abnormality of the heart which results in increased intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise.(McDonagh et al., 2021)Diverse definitions have been developed for different purposes, ranging from 'textbook' definitions of HF, which are typically focused on pathophysiology, to case definitions such as the Framingham criteria(Ponikowski et al., 2016) that are primarily used in biomedical research.(McKee et al., 1971)

Several definitions of HF abound in current medical literature. These include definitions from the American College of Cardiology/American Heart Association (ACC/AHA), (Yancy et al., 2013) Heart Failure Association / European Society of Cardiology (HFA/ESC), (Ponikowski et al., 2016)and Japanese Heart Failure Society (JHFS)(Tsutsui et al., 2019) guidelines (*Table 1)*. Although these differ in some details, all identifies HF as a *clinical syndrome*, all require the presence of at least some of the cardinal symptoms of HF including dyspnoea, fluid retention/edema, fatigue, activity intolerance and exercise limitation; and all these definitions require some form of structural or functional heart disease at the pathogenetic level.

ACCF/AHA, 2016(Yancy et al., 2013)	**HF is a complex clinical syndrome which results from structural or functional impairment of ventricular filling or ejection of blood. The classical manifestations of HF are dyspnoea and fatigue, which may restrict exercise tolerance, or fluid retention, which may cause pulmonary and/or splanchnic congestion and/or peripheral edema. Few of the patients have exercise intolerance but little evidence of fluid retention, whereas others complainprimarily of edema, dyspnoea, or fatigue.**
ESC, 2016(Ponikowski et al., 2016)	**Heart Failure is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, fatigue, and ankle swelling) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral edema) caused by a structural and/or functional cardiac abnormality, resulting in reduced cardiac output and/or elevated intracardiac pressures at rest or during stress.**
JCS/JHFS, 2017(Tsutsui et al., 2019)	**HF is a clinical syndrome consisting of dyspnoea, malaise, swelling and/or decreased exercise capacity due to the loss of compensation for cardiac pumping function due to structural and/or functional abnormalities of the heart**.

Table1: **Heart failure definitions in contemporary clinical practice guidelines**

Gaps in current definitions of heart failure

The definitions discussed above have several inherent limitations. Firstly, they are difficult to apply in public health or epidemiological settings, because of the subjectivity of the symptoms. Moreover, the difficulty (invasive nature of investigations) or unreliability of measurements of cardiac output or filling pressures makes their use impractical in general clinical settings. A definition to be useful in clinical care settings should be assessable easily, with relatively low inter-observer variability. Similarly, the Framingham criteria, which were developed for a purely research purpose, are now considered insufficiently specific for adoption in the clinical setting.

Natriuretic peptides like N-terminal pro-B-type natriuretic peptide (NT-proBNP) and B-type natriuretic peptide (BNP) are elevated in most forms of HF. They are of paramount importance in diagnosing HF, especially when the diagnosis is mired in uncertainty and doubt. These biomarkers are widely used in contemporary practice guidelines, have the highest class of recommendation to support or exclude a diagnosis of HF, (Yancy et al., 2017) in contemporary practice guidelines, but are notably absent from most definitions of HF. Accordingly, the 2017 ACC/AHA/HFSA focused update of the guidelines for the management of HF incorporated recommendations for natriuretic peptide-based screening in the prevention of HF as a Class IIa recommendation. Similarly, high-sensitivity cardiac troponin levels are associated with future development of incident HF in the general population (deFilippi et al., 2010; Saunders et al., 2011) and in those with evidence of cardiotoxicity or cardiac injury in high-risk populations(Avila et al., 2018) allowing for treatment strategies to prevent development of HF.

The usual pattern of HF includes episodes of clinical worsening, often associated with adverse events or episodes of hospitalization.(Butler et al., 2014)Over the years, the concept of worsening HF has been spanned to include patients who require escalation of outpatient therapies, such as diuretics, even without a hospitalization.(Greene et al., 2018) It has been well established that the need for intensifying diuretic therapy, connotes a worse prognosis than a situation which does not mandate intensification of therapy. Accordingly, it is expected that a definition of HF will incorporate such dynamic measures of clinical worsening or improvement, so as to make the definition more acceptable and useful in clinical perspectives.

Revised Universal definition of Heart Failure

Keeping the above in mind the **Universal definition and classification of heart failure: a report of the Heart Failure Association of the European Society of Cardiology, the Heart Failure Society of America, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure** was published in 2021.(Bozkurt et al., 2021)

In this universally accepted document, HF was defined as **a clinical syndrome with current or prior characteristic symptoms and/or signs caused by a structural and/or functional cardiac abnormality (as determined by EF <50%, abnormal cardiac chamber enlargement,**

E/E′ >15, moderate/severe ventricular hypertrophy or moderate/severe valvular obstructive or regurgitant lesion) and corroborated by *at least one* of the following:

- Elevated natriuretic peptide levels (Table 2)
- Objective evidence of cardiogenic pulmonary or systemic congestion by diagnostic modalities such as imaging (e.g. by chest X-ray or elevated filling pressures by echocardiography) or haemodynamic measurement(e.g. right heart catheterization, pulmonary arterycatheter) at rest or with provocation (e.g. exercise)

	Ambulatory	**Hospitalized / decompensated**
BNP, pg/mL	≥35	≥ 100
NT-proBNP, pg/mL	≥ 125	≥ **300**

Table 2: Cut off values of BNP and NT-proBNP for the diagnosis of HF.

The same group of authors freshly classified heart failure according to ejection fraction. This classification was not only based upon prognostic implications of the EF subpopulations, but also on the therapeutic implications of specific EF categories. Several trials have already established that EF may shift from one sub-group to another, and EF sub-groups respond variably to life prolonging therapies(Pfeffer et al., 1992, 2003; Pitt et al., 2003) The new classification system was based on this dynamic therapeutic and prognostic concept (Table 3).

HF with reduced EF (HFrEF)	HF with LVEF ≤40%
HF with mildly reduced EF (HFmrEF)	HF with LVEF 41–49%
HF with preserved EF (HFpEF)	HF with LVEF ≥50%
HF with improved EF (HFimpEF)	HF with a baseline LVEF ≤40%, a ≥10% increment in baseline LVEF, and a second measurement of LVEF of more than 40%.

Table 3: Classification of HF according to ejection fraction

Epidemiology of HF

With rapid strides made in the diagnosis and treatment of HF, the incidence of HF In developed countries may be falling; however, this decline is counterbalanced by ageing, and the overall incidence of HF is increasing globally.(Conrad et al., 2018; Dunlay and Roger, 2014; Roth et al., 2015; Savarese and Lund, 2017) Currently, the incidence of HF in Europe is about three in 1000 person-years (all age-groups) or about five in 1000 person-years in adults.(Brouwers et al., 2013; Meyer et al., 2015) The prevalence of HF may be as high as 12% in adults.(James et al., 2018; Mosterd and Hoes, 2007; Roger, 2013; Smeets et al., 2019; Virani et al., 2020)HF is a clinical syndrome and passes through various stages of severity, ranging from asymptomatic at risk individuals to overt cases requiring immediate hospitalizations. As studies usually include only diagnosed HF cases, the prevalence of true HF is likely to be higher.(van Riet et al., 2014) The prevalence also increases with age: from around 1% for aged <55 years to >10% in those aged 70 years or over.(Benjamin et al., 2018; Bibbins-Domingo et al., 2009; Ceia et al., 2002; van Riet et al., 2016)

HF in India

Sparse population data are available from developing nations regarding presentation, management, and outcomes of patients hospitalized with HF.(Sivadasan Pillai and Ganapathi, 2013) Available data in India are based on extrapolations from heart failure risk factor prevalence data in India on ischemic heart disease, hypertension, diabetes, obesity, and rheumatic heart disease to estimate HF incidence and prevalence.(Pais and Xavier, 2011) The Trivandrum Heart Failure Registry (THFR) was the first organized HF registry in India published in 2015. In comparison with other international publications like the American ADHERE registry, the Korean registry, and the European Society of Cardiology registry, patients in the THFR were 8–10 years younger.(Adams et al., 2005; Maggioni et al., 2013; Youn et al., 2012) On a similar note, the Kerala ACS and CREATE registries show that Indians develop acute coronary events at a younger age.(Mohanan et al., 2013; Xavier et al., 2008)

Furthermore, the age distribution in Indian patients is different from the Western world. While patients aged less than 65 years constitute only 57% of the population in the THFR registry, this group comprises only 29% of the ADHERE registry.(Adams et al., 2005) More than one quarter

of the ADHERE registry patients and more than one-third of the Japanese ATTEND registry patients are aged over 85 years, compared with only 4% of patients in the THFR.(Sato et al., 2013)While the sex ratio in the THFR population is skewed with a male predominance of 69%, the proportion of women in the ADHERE registry, the ESC registry, and the Japanese ATTEND registry are 52%, 37%, and 42%, respectively.(Adams et al., 2005; Maggioni et al., 2013; Sato et al., 2013)

Heart failure with preserved ejection fraction (HFpEF)

HFpEF is defined as patients with HF with documented left ventricular ejection fraction (LVEF) equal to or more than 50%.(Bozkurt et al., 2021)

Globally, HFpEF accounts for close to 50% of patients presenting with HF. As per the registry data like Trivandrum Heart Failure Registry and ASIAN-HF, the proportion of HFpEF in our country is approximately 19–25%, which is much lower as compared to that of western population.(Harikrishnan et al., 2015; Tromp et al., 2019) There is a possibility that many cases go undiagnosed in developing countries like India. The mean age of presentation of HFpEF patients from India is around 58–68 years, which is about 10 years younger than the data reported from the West.

HFpEF is characterized by elevated left ventricular filling pressures and/or reduced cardiac output either at rest or on exertion. Cardiac output is maintained at the cost of abnormally elevated filling pressure which is responsible for the symptoms and signs. Neurohumoral activation (sympathetic and renin-angiotensin-aldosterone system activation) is present only in a group of HFpEF patients, unlike in patients with heart failure with reduced ejection fraction (HFrEF).(Vergaro et al., 2019)

The diagnosis of HFpEF requires a clinicopathological correlation. The presence of symptoms and signs of HF along with elevated biomarkers, the demonstration of preserved LVEF (≥50%), and the documentation of diastolic dysfunction on echocardiogram are essential prerequisites. Cardiac catheterization is the gold standard procedure for confirmation of diagnosis, but this is not feasible in resource limited settings. On the background of appropriate clinical features, a PCWP of ≥15 mm Hg (at rest) or left ventricular end-diastolic pressure (LVEDP) ≥16 mm Hg (at

rest) is generally considered diagnostic. If resting echocardiographic findings and laboratory parameters are equivocal, diastolic stress test is recommended. (McDonagh et al., 2021)

An electrocardiogram and a chest X-ray along with blood tests including blood cell counts, renal function test, thyroid function test, glycosylated hemoglobin, lipid levels, iron studies, and biomarkers like B-type natriuretic peptide (BNP/NT-proBNP) and troponin, are advised for all patients with suspected HFpEF. Transthoracic echocardiogram with detailed evaluation for cardiac chamber enlargement, left ventricular hypertrophy, diastolic function assessment, and pulmonary hypertension is essential in the workup. Patients with suspected infiltrative cardiomyopathy, hemochromatosis, or hypertrophic cardiomyopathy merit a CMR evaluation.

A writing committee of the HFA of the ESC has produced an updated consensus recommendation.(Paulus et al., 2007) This is reflected in the HFA–PEFF diagnostic algorithm (Table 4). Its key features are (i) the concept that identification of HFpEF involves all levels of care, starting from general practitioners, internists, general cardiologists, HF specialists, to invasive cardiologists; (ii) accordingly, a stepwise diagnostic approach from initial clinical assessment to more specialized tests should be useful; (iii) since the diagnosis is not always straightforward, it has been recommended to integrate distinct parameters from complementary diagnostic domains into a new diagnostic score; (iv) for patients with an inconclusive score, confirmatory diagnosis (or exclusion) will require invasive hemodynamics and/or invasive or non-invasive exercise stress tests; and (v) underlying alterations in pathophysiological process (such as chronotropic incompetence, reduced LV compliance) and specific etiologies have to be considered. A precise diagnosis is increasingly important since new targeted therapies are becoming available for defined subsets of HFpEF patients.

HFA – PEFF algorithm for the diagnosis of HFpEF		
P	Initial workup (Step 1(P): Pretest assessment)	Symptoms and Signs of HF, Comorbidities / Risk factors, ECG, standard echocardiography, Natriuretic peptides, Ergometry / 6 minute walk test or cardiopulmonary exercise testing
E	Diagnostic workup (Step 2(E):Echocardiographic and Natriuretic peptide score)	Comprehensive echocardiography, Natriuretic peptides, if not measured in Step 1
F1	Advanced workup (Step 3(F1): Functional testing in case of uncertainty)	Diastolic stress test: Exercise stress echocardiography, Invasive hemodynamic measurements
F2	Etiological workup (Step 4(F2): Final etiology)	CMR, cardiac or non-cardiac biopsies, Scintigraphy / CT / PET, Genetic testing, specific laboratory tests

Table 4A: HFA-PEFF diagnostic algorithm. Overview of the diagnostic heart failure with preserved ejection fraction steps 1–4 (P–F). CT, computed tomography; PET, positron emission tomography.

In this PEFF algorithm proposed by the European Society of Cardiology (ESC), a score of 2 – 4 (borderline) warrants stress testing or invasive hemodynamic testing and a score ≥5 points is diagnostic of HFpEF (Table 5).(Pieske et al., 2019) If key haemodynamic abnormalities are identified on stress test, a definite diagnosis of HFpEF may be made. Invasive haemodynamic measurements at rest or during exercise are essential to diagnose HFpEF if diagnostic uncertainty remains after diastolic stress test.

	Functional	Morphological	Biomarker (SR)	Biomarker (AF)
Major	Septal e'<7cm/s or Lateral e' <10cm/s Average E/e' >15 or TR velocity >2.8m/s (PASP > 35 mmHg)	LAVI > 34mL/m^2 or LVMI ≥149/122g/m^2 and RWT >0, 42 #	NT – proBNP > 220pg/mL Or BNP > 80pgmL	NT – proBNP > 660pg/mL Or BNP > 240pgmL
Minor	Average E/e' 9 – 14 Or GLS < 16%	LAVI 29 – 34 mL/m^2 Or LVMI >115/95g/m^2 Or RWT > 0, 42 Or LV wall thickness ≥12mm	NT – proBNP > 125 - 220pg/mL Or BNP 35 - 80pgmL	NT – proBNP 365 - 660pg/mL Or BNP 105 - 240pgmL
Major criteria: 2 points		≥ 5 points: HFpEF		
Minor criteria: 1 point		2 – 4 points: Diastolic stress test or Invasive Hemodynamic measurements warranted to confirm the diagnosis of HFpEF		

Table 4B: Echocardiographic and natriuretic peptide based scoring system for the diagnosis of HFpEF

Taking a step further, the 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction has formulated the H2FPEF scoring system.(Kittleson et al., 2023) The H2FPEF score was derived and validated using a gold-standard reference of invasive exercise hemodynamic measurements and is the more practical system for use by clinicians (Table 6). The 6 components of the H2FPEF score consist of information that is readily accessible: Heavy (body mass index [BMI] >30 kg/m^2), Hypertension (on 2 or more antihypertensive medications), atrial Fibrillation, Pulmonary hypertension (estimated pulmonary artery systolic pressure >35 mm Hg on Doppler echocardiography), Elder (age >60 years), Filling pressures (E/e' >9 on Doppler echocardiography). A score of 6 or more is highly suggestive of HFpEF.

H	Heavy (BMI > 30 kg/m2)	**2**
H	On ≥2 anti-hypertensives	**1**
F	Atrial fibrillation	**3**
P	Pulmonary hypertension (PASP > 35 mmHg on Doppler echocardiography)	**1**
E	Elder age (>60 years)	**1**
F	Filling pressure (E/e' > 9 on Doppler echocardiography)	**1**

Table 5: HFpEF Diagnostic Scoring System, ACC, 2023

The diagnosis and prognostication of HFpEF remains a challenging proposition. Recent studies suggest that modern and digital imaging methods like CMR may be useful for diagnosis and for defining pathophysiology.(Omar et al., 2017; S et al., 2022) However, long-term studies in large populations are needed to unravel which features best predict clinical outcomes and responses to treatment.

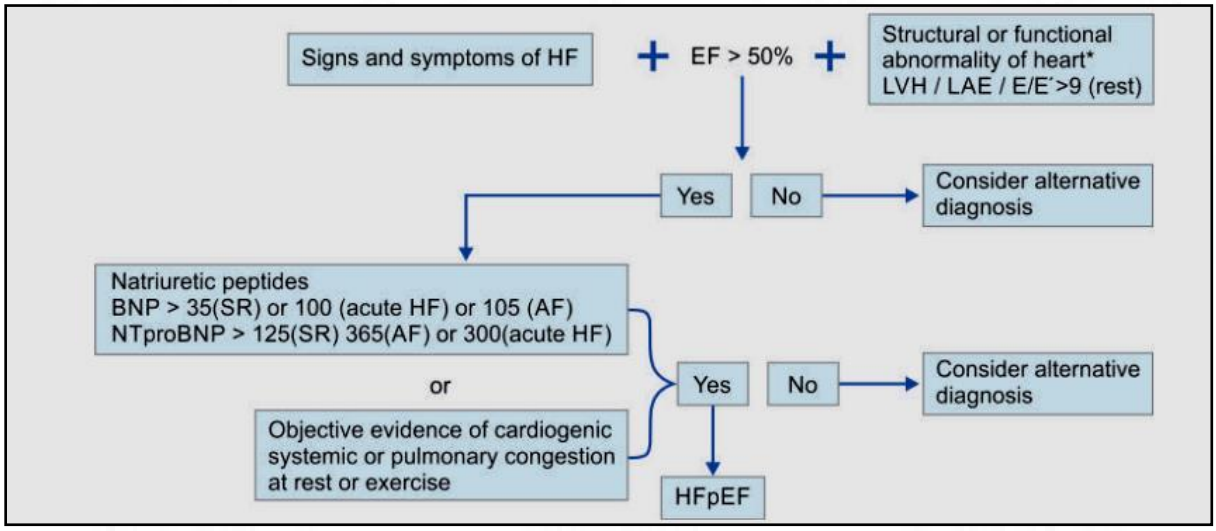


Fig A: Algorithm for diagnosis of HFpEF. *LV mass index ≥95 gm/m^2 (female), ≥115 gm/m^2 (male), relative wall thickness >0.42 LA volume index >34 mL/m^2 (SR) >40 mL/m^2 (AF) PA systolic pressure—TR velocity at rest >35 mm Hg/>2.8 m/s at rest. On exercise TR velocity >3.4 m/s, E/E' >15; BNP, B-type natriuretic peptide; E/E' ratio, early filling velocity on mitral inflow Doppler/early relaxation velocity on tissue Doppler; LA, left

atrial; LV, left ventricular; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PA, pulmonary artery; SR, sinus rhythm; TR, tricuspid regurgitation.(Pieske et al., 2019)

Diagnosis of HFpEF

The diagnostic tests which are recommended for the assessment of patients with suspected chronic HF are as following:

(1) Electrocardiogram (ECG). An ECG, which is normal, makes the diagnosis of HF highly unlikely.(Sanchez-Martinez et al., 2018) The ECG may unmask abnormalities such as AF, Q waves, LV hypertrophy (LVH), and a wide QRS complex that increase the likelihood of a presence of HF and also may guide therapy.

(2) Measurement of NP is recommended, if available. A plasma concentration of BNP <35 pg/mL, NT-proBNP <125 pg/ mL, or mid-regional pro-atrial natriuretic peptide (MR-proANP) <40 pmol/L make a diagnosis of HF unlikely.(Mant et al., 2009) Elevated plasma concentrations support a diagnosis of HF, are useful for prognostication, and may guide further cardiac investigation.(Gohar et al., 2019; Schwitter et al., 2013) However, it should be noted that there are many causes of an elevated NP—both CV and non-CV—that might reduce their diagnostic accuracy. These include AF, increasing age, and acute or chronic kidney disease.(Roberts et al., 2015) Conversely, NP concentrations may be disproportionately low in obese patients.(Mueller et al., 2019)

(3) Echocardiography is recommended as pivotal investigation for the assessment of cardiac function. As well as the determination of the LVEF, echocardiography also provides information on other parameters such as chamber size, ventricular hypertrophy, regional wall motion abnormalities (which may indicate underlying CAD, Takotsubo syndrome, or myocarditis), RV function, pulmonary hypertension, valvular function, and markers of diastolic function.(Galderisi et al., 2017; Madamanchi et al., 2014)

(4) A chest X-ray is advised to investigate other potential causes of breathlessness (e.g. pulmonary disease). It may also provide supportive evidence of HF (e.g. pulmonary congestion or cardiomegaly)

(5) CMR imaging with late gadolinium enhancement (LGE), T1 mapping and extracellular volume can identify myocardial fibrosis/scar, which are mostly subendocardial for patients with ischemic heart disease (IHD) in contrast to the mid-wall scar typical of dilated cardiomyopathy (DCM). In addition, CMR allows myocardial characterization in diseases like myocarditis, amyloidosis, sarcoidosis, Chagas disease, Fabry's disease, LV non-compaction CMP, hemochromatosis, and arrhythmogenic cardiomyopathy (AC).(Gonzalez and Kramer, 2015; Lancellotti et al., 2017)

(6) Computed tomography coronary angiography (CTCA) can be considered in low and intermediate pre-test probability patients of coronary artery disease, or those with equivocal non-invasive stress tests to exclude the diagnosis of CAD.(Messroghli et al., 2017)

(7) Single-photon emission CT (SPECT) can also be used to assess myocardial ischaemia and viability, myocardial inflammation or infiltration. Technetium (Tc)-labelled bisphosphonate scintigraphy has shown high sensitivity and specificity for imaging cardiac transthyretin amyloid.(Knuuti et al., 2020)

Non-invasive imaging plays a key role in the evaluation and management of a patient with a clinical diagnosis of heart failure.(Witteles et al., 2019)A detailed recording of the clinical history, the determination of signs and symptoms, and meticulous physical examination are indispensable steps in the evaluation of a patient with suspected or known heart failure. Thereafter, non-invasive imaging is used to further characterize the heart failure, with the aim of confirming or establishing the etiology, classifying the type and stage of heart failure, targeting therapies and assigning a prognosis.

Global and regional left ventricular function

Ejection fraction is the most often used index to assess global left ventricular systolic function.(Ponikowski et al., 2016; Yancy et al., 2013) When the left ventricular ejection fraction (LVEF) is less than 40%, there is universal consensus that this indicates heart failure with reduced ejection fraction (HFrEF). When the LVEF is >50%, this is termed as heart failure with preserved ejection fraction (HFpEF), and an LVEF of 41–49% represents heart failure w

ith medium range ejection fraction (HFmrEF, according to the European Society of Cardiology guidelines) or borderline ejection fraction (HFpEF-borderline, according to the American College of Cardiology/American Heart Association guidelines). Some of the patients with a LVEF of >40% may be those whose ejection fraction was previously <40%(i.e. patients who have improved from HFrEF to HFpEF-borderline or even HFpEF).(Bozkurt et al., 2021) This classification has prognostic significance, determines the selection of appropriate drug therapy and aids in decision making on the timing and appropriateness of device therapy.

LVEF is most commonly measured or estimated by 2-D echocardiography. Traditional echocardiography has the limitations of inadequate acoustic windows, and microbubble contrast echocardiography which overcomes this impediment cannot overcome the fundamental geometric assumptions made in 2-D imaging, and the intrinsic issue of operator variability. Cardiac magnetic resonance (CMR) is currently the alternative technique for the measurement of ejection fraction, and radionuclide ventriculography being the alternative when CMR is not available or feasible.

Regional function is most commonly assessed by the visual examination of myocardial thickening and wall motion. The degree of abnormality is classified as hypokinetic, akinetic or dyskinetic muscle with scores assigned to each abnormality. The sum of the scores assigned to each region is then used as a semiquantitative measure of the severity, with higher scores representing more severe regional dysfunction. The presence of significant regional dysfunction in the setting of HFrEF, HFmrEF or HFpEF generally points to an ischemic etiology for heart

failure. However, global left ventricular dysfunction in heart failure may also be associated with regional dysfunction. Echocardiography and CMR are the two most useful imaging modalities to assess regional myocardial function in terms of thickening and motion.

Left ventricular size and shape

Left ventricular size can be measured as a dimension or volume. The former is practical and simple, and the latter is a better descriptor of size than a dimension, but requires more data and takes time to compute. The measurement of left ventricular volume is especially relevant when there is significant regional dysfunction. Left ventricular dimension as an index of left ventricular size is not recommended in the latter situation. Both end diastolic and end systolic left ventricular size and volume has prognostic significance and are indices that can be used to assess the effectiveness of heart failure therapies.(Patel et al., 2013) Left ventricular global shape measured as the sphericity index or regional shape measured as endocardial curvature are also critical determinants of global and regional left ventricular function but whether these should be measured selectively or routinely is not currently established. Thus, only the measurement of left ventricular size is presently recommended in routine practice. 2-D echocardiography is used to measure left ventricular dimensions and volumes, although the measured volumes are smaller than those measured with CMR. Contrast echocardiography improves the accuracy of 2-D echocardiography for measurement of volumes, but they still prove to be smaller than CMR volumes and have the disadvantage of geometric assumption for the calculation of volume. CMR imaging is the reference standard for left ventricular volume and when accurate, reproducible left ventricular volume measurements are necessary for clinical purposes. 3-D echocardiography is superior to 2-D echocardiography and may prove to be a practical alternative to CMR, at least in those with adequate acoustic windows.

Myocardial morphology and function

Three key attributes of myocardial morphology that can be assessed by imaging include myocardial thickness, myocardial morphology and myocardial scarring and fibrosis. Myocardial

thickness is the mass of the myocardium bounded internally by the endocardium and externally by the epicardium. There are regional variations in myocardial thickness with the apex of the heart being the thinnest part of the left ventricular myocardium. Myocardial thickness is a key component of left ventricular mass, which in turn is a key determinant of prognosis in heart failure. The ratio of myocardial thickness to the left ventricular cavity size (volume) is an index of regional wall tension that plays a significant role in left ventricular remodeling.(Marwick, 2018)

Assessment of myocardial morphology focuses on the extent of excessive trabeculations. These shallow fingerlike projections of the endocardium are normally present in the adult left ventricle at the apex, lateral, inferior and posterior walls, while non-trabeculated part are the interventricular septum and the anterior walls in the adult. Excessive trabeculation in regions where there is usually some trabeculation or presence of trabeculation in areas where there is usually none may be indicative of a cardiomyopathy. Conversely, excessive trabeculation may merely be a marker of extreme left ventricular dilatation that causes exaggeration of the normally present trabeculation. Myocardial trabeculations play a role in myocardial deformation (strain) and excessive, abnormal trabeculations may potentially contribute to abnormal myocardial strain and adverse left ventricular remodeling.

The presence, extent and amount of myocardial scarring and fibrosis is crucial to left ventricular function. Scarring usually follows injury to the myocardium such as infarction: the loss of myocytes triggers fibroblast activation that results in replacement fibrosis, but the total myocardial mass is decreased and in general there is thinning of the myocardium.

Alternatively, increased myocardial stress such as hypertension can activate the fibroblasts, which causes diffuse interstitial (reactive) fibrosis and expansion of the extracellular volume, resulting in increased total myocardial mass and myocardial hypertrophy. Alternatively, cell death can result in myocyte loss, which is then replaced by replacement fibrosis, maintaining increased myocardial mass and myocardial hypertrophy. These structural changes are essential determinants of natural history and clinical outcomes of heart failure syndromes. They influence the selection and success of therapeutic strategies, and provide targets for newer therapies.(Konstam and Abboud, 2017)

Myocardial function is measured as strain. Although myocardial strain has been previously measured by CMR in normal and abnormal left ventricles, it has only recently evolved into a practical index of myocardial function. Myocardial strain is an estimate of myocardial deformation, which is a sensitive imaging parameter of myocardial disease than the commonly used ventricular EF. Although myocardial strain is very often evaluated by using echocardiography because of its easy availability, CMR is increasingly used for this purpose. CMR utilises feature tracking (FT), which involves post-processing of cine MR images. Other CMR strain techniques require special sequences, including myocardial tagging, displacement encoding with stimulated echoes, strain-encoded imaging, and tissue phase mapping. The complex motion of the heart can be translated into longitudinal, circumferential or radial strain, and torsion. Myocardial strain measurements include strain rate, velocity, torsion, displacement, and torsion rate. The reference ranges vary widely on the imaging technique, software used for analysis, operator, patient demographics, and hemodynamic factors. In chemotherapy-induced cardiotoxicity, CMR myocardial strain can help to identify left ventricular dysfunction before having a decline in ejection fraction. Strain is also important for identifying patients with inter and intra ventricular dyssynchrony who may benefit from resynchronization therapy. CMR myocardial strain is also useful in CAD, cardiomyopathies, pulmonary hypertension, and congenital heart disease.(Konstam et al., 2011)

Myocardial ischemia or viability

Coronary artery disease (CAD) leading to myocardial ischemia or infarct remains the most common etiology for HF. Obstructive CAD and non- obstructive CAD arising from microvascular dysfunction are both treatable causes of ischemic HF, and testing for myocardial ischemia is critical in the initial assessment of HF. In addition, the assessment of myocardial viability may be important when making decisions about revascularization in the setting of ischemic heart failure and significant left ventricular dysfunction (LVEF < 30%).(Rajiah et al., 2022)

Stress and rest single photon emission computed tomography (SPECT) or positron emission tomography (PET) are the most commonly used methods to assess myocardial ischemia and

viability in heart failure. The assessment of the presence and severity of myocardial ischemia by both these techniques has proven their diagnostic and prognostic value in patients with heart failure.(Bax and Delgado, 2015; Djaileb et al., 2019) CT coronary artery calcium score (CACS) and coronary computed tomography angiography (CCTA) are emerging as useful tests that provide adjunctive, and often useful, information on the probability of the presence of obstructive CAD and/or coronary plaque morphology.

Stress and rest echocardiography and CMR are the other two non-invasive tests for the assessment of myocardial ischemia. Dobutamine or vasodilator stress echocardiography have both been shown to be useful methods to evaluate myocardial ischemia and viability. In addition, exercise echocardiography can be used to test for myocardial ischemia. These echocardiographic based tests have been shown to have good diagnostic and prognostic value in patients with left ventricular dysfunction. The addition of contrast has further extended their utility through the enhancement of endocardial borders and by providing information on microvascular integrity (myocardial contrast echocardiography). The feasibility and reliability of myocardial contrast echocardiography, however, has not been demonstrated in large studies and is not recommended. Despite the plethora of data with stress echocardiography, a challenge is the assessment of ischemia or viability in left ventricular dysfunction with thinned out walls. Thus, CMR has emerged as an alternative to echocardiography and is often the second line test after SPECT–PET. Stress and rest CMR myocardial perfusion imaging (MPI) also has excellent spatial resolution for the evaluation of wall thickening, which improves the reliability of the test.

Left atrium and right ventricle

The size of the left atrium is an independent predictor of outcomes in heart failure.(Löffler and Kramer, 2018) It is also an important marker of abnormalities in diastolic filling of the left ventricle in all categories of heart failure. Similarly, left atrial function and strain are emerging as sensitive indicators of myocardial dysfunction and predictors of outcome in heart failure. However, these measurements will need further investigations before they are recommended as routine measurements in patients with heart failure. Currently, measurement of left atrial volume on bi-plane echocardiography is implemented as an adjunct assessment of left ventricular diastolic dysfunction along with tissue Doppler to estimate prognosis in heart failure. 3-D

echocardiography and CMR are alternative techniques that are performed selectively to evaluate the left atrial volume.

The right ventricular ejection fraction (RVEF) is a powerful indicator of outcomes in left sided heart failure.(Rossi et al., 2009) CMR is the preferred technique to measure the RVEF, but it is not practical in all patients with heart failure. Therefore, a number of 2-D echocardiographic indices of right ventricular systolic function have been used as a surrogate for RVEF, and many of these have shown good correlation with RVEF. These indices have also been prognostically valuable. 3-D echocardiography holds promise to measure RVEF, but this needs further validation and the feasibility for routine use remains to be determined. Right ventricular myocardial strain is another parameter that may be incremental to RVEF or even superior to RVEF in the prognostication of heart failure, but this needs to be confirmed in future studies.

Valve disease

Secondary or functional mitral regurgitation (MR) is the most common valve disease in the heart failure population. Some degree of mitral regurgitation is seen in the majority of patients with heart failure, with severe mitral regurgitation being present in about a third of the patients with systolic heart failure. While there is a good understanding of the mechanisms of secondary mitral regurgitation, the treatment strategies for this are more controversial and are still being debated. However, there is universal agreement that significant functional mitral regurgitation worsens prognosis in heart failure and, if unresolved with maximum tolerated guideline directed medical therapy, other interventions must be considered for the optimal treatment of mitral regurgitation.(Ghio et al., 2001) Among the surgical options, mitral valve replacement has been shown to be better than repair as the former is more likely to prevent recurrent mitral regurgitation. Cardiac resynchronization therapy has also been shown to be useful to reduce or abolish mitral regurgitation. More recently, catheter based therapies for mitral regurgitation such as repair with a mitral clip or other annuloplasty device, and replacement with specifically designed valves for the mitral position, have shown promise. These minimally invasive transcatheter therapies may yet transform the solutions for a problem for which there are limited options, if any.

Functional tricuspid regurgitation is being increasingly recognized as an important contributor to morbidity in heart failure. While the data are compelling, the options for treatment are even more limited than those for functional mitral regurgitation, with surgical repair being the only option until recently. However, surgery for functional tricuspid regurgitation alone was not enthusiastically embraced given that many of these patients had varying degrees of right ventricular systolic dysfunction and did not benefit from the abolishment of tricuspid regurgitation. However, the emergence of transcatheter devices for tricuspid valve repair is promising and hence routine assessment of tricuspid regurgitation may become essential in heart failure.

Cardiomyopathy

Cardiomyopathy is an intrinsic myocardial structural disorder of that may lead to ventricular dysfunction and can progress to clinical heart failure. It is a major public health issue, affecting more than 5.8 million people in the United States of America and more than 23 million people worldwide.(Nasser et al., 2017)Based on their morphological and haemodynamic characteristics, cardiomyopathies have historically been divided into three major categories: dilated cardiomyopathy, hypertrophic cardiomyopathy and restrictive cardiomyopathy.

Echocardiography is the on-the-go imaging technique used for the initial diagnosis and management of cardiomyopathy. However, other imaging modalities, including nuclear cardiology (myocardial perfusion imaging, MPI with either SPECT or PET), cardiac magnetic resonance (CMR) imaging and cardiac computed tomography (CCT), play an important role, depending on the underlying etiology of the cardiomyopathy.

As the first line imaging procedure, echocardiography delineates several important pathophysiological mechanisms, such as systolic versus diastolic left ventricular dysfunction, valvular and pericardial diseases, and probable non-ischaemic versus ischaemic cardiomyopathy. The latter can be further investigated with myocardial perfusion imaging (MPI) and CMR to establish the presence of inducible myocardial ischemia and scarring.(Bui et al., 2011) Coronary computed tomography angiography (CCTA) helps to establish the presence of obstructive CAD.(Mahrholdt et al., 2005; Nagueh et al., 2017) Multimodality imaging is particularly useful in the differential diagnosis of HFpEF that can be secondary to severe tricuspid regurgitation,

restrictive cardiomyopathy, constrictive pericarditis and hypertrophic cardiomyopathy. The role of multimodality imaging in restrictive cardiomyopathies has been recently reviewed.

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy is a genetic myocardial disorder, phenotypically affecting 0.2% of the general adult population, independent of sex and ethnicity. The typical pathological findings of the disease are myocyte hypertrophy and hyperplasia, myocyte disarray, small vessel disease and fibrosis. The clinical features of hypertrophic cardiomyopathy range from a benign, asymptomatic condition with a normal life expectancy to being the most frequent cause of sudden cardiac death (SCD) in the young age group and in athletes under 35 years of age. Heart failure and atrial fibrillation are the most relevant complications.(Authors/Task Force members et al., 2014; Habib et al., 2017; Maron, 2002) Echocardiography is recommended in all patients with hypertrophic cardiomyopathy on diagnosis and during follow-up. CMR can be considered depending on the clinical presentation and can provide useful information on morphology and architecture. CCTA and MPI can be used to exclude CAD and myocardial ischemia. PET is the best method for evaluating microvascular ischaemia.(Cardim et al., 2015)

Dilated cardiomyopathy

Dilated cardiomyopathy is the most common form of non-ischaemic cardiomyopathy and is phenotypically characterized by dilatation of cardiac chambers with associated left and right ventricular systolic dysfunction, often with concomitant functional mitral regurgitation. Transthoracic echocardiography findings that may suggest a specific aetiology of dilated cardiomyopathy include focal posterolateral akinesis or dyskinesis suggestive of dys trophin related dilated cardiomyopathy or mild dilatation with akinetic or dyskinetic segments in a non-coronary distribution suggestive of inflammatory or infectious aetiologies. CMR may suggest a specific aetiology, especially hemochromatosis, sarcoidosis and myocarditis. CMR also permits the localization of involved segments amenable to endomyocardial biopsy.

SPECT and PET myocardial perfusion scintigraphy can quantify myocardial perfusion to exclude an ischemicetiology. Nuclear imaging in dilated cardiomyopathy can demonstrate either a homogeneous distribution of blood flow or patchy (non-vascular) perfusion abnormalities on MPI, and uniform glucose metabolism on 18F-fluorodeoxyglucose (FDG) PET images. This is in

contrast toischemic cardiomyopathy, where discrete reduction in perfusion and/or reduced glucose utilization is found inleft ventricular segments corresponding to a coronary distribution.

Restrictive cardiomyopathy

Restrictive cardiomyopathy (RCM) is characterized by impaired diastolic filling with restrictive physiology, reduced diastolic volume of either or both ventricles, normal or near normal ventricular systolic function and wall thickness, and biatrial enlargement.(Sciagrà, 2016) Tissue characterization with CMR allows the further characterization of other underlying disorders potentially contributing to the restrictive physiology. PET is the most sensitive modality for identifying the areas of increased 18F-FDG uptake indicative of inflammation.

Magnetic resonance imaging (MRI) allows the accurate non-invasive and radiation free evaluation of the heart and vascular structures, with high contrast and large field of view without the restriction of an acoustic window. CMR is currently the standard of reference for the measurement of chamber volumes, and its high accuracy in tissue characterization has an excellent correlation with biopsy. It is therefore an imaging technique particularly suitable for serial studies and the close monitoring of changes in chamber dimensions or the severity of valvular abnormalities that can impact clinical management.

Basics of magnetic resonance imaging

Magnetic resonance data are acquired from the properties in hydrogen nuclei, which are present in water and fat within tissue. Each proton acts like a tiny magnet because of an intrinsic property known as nuclear spin, which gives rise to a small magnetic field (magnetic moment). The magnetic moments (spins) are naturally randomly oriented so that their magnetic fields do not add but rather cancel one another out. In the presence of a static magnetic field, they tend to align towards or against this field.

The excess of proton magnetic moments combines to form a net magnetic field or net magnetization along the *z* axis of the external magnetic field, becoming the source of the magnetic resonance signal, which is ultimately detected and imaged. The greater the applied magnetic field strength, the greater the excess of protons aligned with the magnetic field and the

more the size of the net magnetization. A typical clinical MRI system will have a magnetic strength of 1.5 T, but 3 T systems are also increasingly available.

To be able to generate a signal, the net magnetization vector is tracked into the transverse plane by applying a small magnetic field rapidly changing at radio frequencies for a small period of time (pulse). The field is applied by a transmitter coil at a particular Larmor frequency (defined by the Larmor equation), determined by the strength of the magnetic field. The gyromagnetic ratio has a value of 42.6 MHz/T for the proton, also known as resonant frequency, as protons only absorb energy (resonate) at this frequency. After a 90° radiofrequency pulse is applied, energy is absorbed, the net magnetization rotates away from the longitudinal direction into the transverse plane (transverse magnetization) and the longitudinal magnetization becomes zero. The magnetization then realigns back with the main magnetization vector), which is called longitudinal (T1) relaxation. The value of T1 is the time it takes for the longitudinal magnetization to reach 63% of its final value and is characteristic of specific tissues; it is the source of contrast in T1 weighted images. After the radiofrequency pulse protons rotate together in a coherent fashion within the *xy* plane, the angle they point to is known as the phase angle. Spins with similar phase angles are considered in phase; when relaxation occurs, there is loss of coherence and they no longer rotate together (and therefore are considered out of phase) and consequently, there is a decay of the transverse magnetization known as T2 relaxation.(Ridgway, 2010; Tummala et al., 2015) All the information acquired during the MRI scan is then transformed into an image using the Fourier transform.

Cardiac magnetic resonance

CMR can acquire a specific fraction of the cardiac cycle in a steady state free precession (SSFP) sequence. It relies on a steady state of magnetization in which the longitudinal and transverse magnetizations are at equilibrium with the use of radiofrequency pulses.(Hendrick, 1994)

To evaluate cardiac function, the standard CMR protocol includes SSFP cine images in a short axis stack from the mitral valve plane through the apex, vertical long axis, four chamber long axis and left ventricle outflow tract long axis. The inclusion of an optional transaxial stack of cines covering the right ventricle should be considered to evaluate right ventricular volumes.(Rajiah and Bolen, 2014)The characterization of myocardial edema is performed in T2

weighted imaging in which blood is seen as a dark signal and edema as a bright signal in the myocardium. These images present some interpretation challenges as they are prone to artifacts caused by slow blood flow. Visual qualitative analysis is usually sufficient in injuries such as acute myocardial infarction and acute myocarditis.(Rajiah and Bolen, 2014; Schulz-Menger et al., 2020)

First pass perfusion is a technique that allows the detection of ischemia; a perfusion defect is seen after the contrast arrival and passage through the left ventricular myocardium. Qualitative analysis is made comparing different regions to identify relative hypoperfusion. These defects should persist beyond the peak of myocardial enhancement and for several R–R intervals. Late gadolinium enhancement (LGE) occurs at least ten minutes after administration and inversion time is set to null the signal of the normal myocardium. LGE occurs in tissue with an increased volume of distribution of gadolinium and slower washout, such as in myocarditis and myocardial infarction. This is a very accurate method to characterize myocardial injury because of its high spatial and contrast resolution.

Blood flow evaluation using CMR

CMR can be used to evaluate blood flow using phase contrast or velocity encoded techniques, based on the principle that moving protons change phase in proportion to their velocity.[152] Velocity encoded cine MRI imaging provides not only a qualitative assessment of flow but also allows an accurate quantification of key haemodynamic parameters such as flow velocity, flow volume and pressure gradients.(Rajiah et al., 2013) The data obtained with velocity encoded MRI are generally reliable and reproducible. However, this comes with the caution that the "velocity and volume of blood flow may be underestimated if the vessel of interest is not imaged in a plane exactly perpendicular to the direction of flow".

Because of the slow acquisition and low spatial resolution compared with computed tomography, the examination of coronary arteries with magnetic resonance angiography is currently not considered appropriate in patients with chest pain symptoms and intermediate pre-test probability of coronary artery disease. The origin and proximal portions of the coronary arteries or dilated vessels can be successfully visualized with CMR, which can subsequently be useful in the diagnosis of anomalous coronary artery origins and in Kawasaki disease.(Hom et al., 2008)

4-D Flow cardiac magnetic resonance

Dyverfeldt et al. describes this as a relatively novel technology that allows a more comprehensive assessment of the pulsatile blood flow through the heart and great vessels (aorta, pulmonary arteries).(Dyverfeldt et al., 2015; Sakuma, 2011) It has a typical spatial resolution of 1.5 mm × 1.5 mm × 1.5 mm to 3 mm × 3 mm × 3 mm, a typical temporal resolution of 30–40 ms, and an acquisition time of approximately 5–25 min. It refers to phase contrast CMR with flow encoding in all three spatial directions that is resolved relative to all three dimensions of space, and to time during the cardiac cycle. The main advantage over 2-D flow imaging is the acquisition of images of flow with higher reproducibility in all spatial dimensions.

Safety considerations with CMR

CMR is contraindicated in patients with certain devices. In 2005, ASTM International developed a set of terms to prevent confusion and accidents. 'MR safe' is used to describe an item with no known hazards in any MRI environment. 'MR conditional' is used to describe an item with no known demonstrated hazards in one specific MRI environment once pre-specified conditions have been applied, for example, the field strength (devices tested at 1.5 T may not be safe at 3 T). 'MR unsafe' is used to describe an item known to pose hazards in all MRI environments and exposure is to be avoided.(Dyverfeldt et al., 2015)

In cases of patients with non-MRI-compatible pacemakers or implantable cardioverter defibrillators, recommendations are to have personnel capable of programming the device be present during the examination. If pharmacological stress is administered, a physician trained in advanced cardiac life support should always be present and life support instruments should be available. Heart rhythm and blood pressure needs to be monitored during the stress and recovery phase.(Woods, 2007)

The use of gadolinium based contrast is contraindicated in patients with stage 4 or 5 chronic kidney disease, as well as in patients with severe acute renal failure, owing to concerns with regard to nephrogenic systemic fibrosis, which might develop in these patients. This risk should be weighed against the clinical benefit of the potential diagnostic information in individual scenarios, as guided by the Radiological Society of North America.(Woodard et al., 2006) These recommendations suggest that depending on the clinical indication, the potential harms of

delaying or withholding group II or group III Gadolinium-based contrast media (GBCM) for an MRI in a patient with acute kidney injury or eGFR less than 30 mL/min per 1.73 m^2 should be balanced against and may outweigh the risk of NSF. Dialysis initiation or alteration is likely unnecessary based on group II or group III GBCM administration.

In summary, CMR has developed into an imaging method with multiple useful

cardiovascular applications. Currently, CMR is the method of choice for the study of ventricular volumes, ventricular function and tissue characterization. The potential hazards of CMRI must be considered, particularly in patients with implanted devices and MRI conditional devices.

T1 Mapping in Heart Failure

Mascherbauer et al studied postcontrast CMR T1 mapping to explore the relationship between extracellular matrix accumulation and outcome in patients with suspected HFPEF.(Mascherbauer et al., 2013) There was a significant difference in T1 time (P<0.01) and biventricular ejection fraction (P<0.01) between patients with confirmed HFPEF and those without confirmed HFpEF. In addition to augmenting the understanding of the pathobiology in HFPEF, the authors found significant association between postcontrast CMR T1 time and outcome in patients with HFPEF (hazard ratio, 0.99 [95% confidence interval: 0.98–0.99]; P=0.046), and from this the authors suggest its potential role as a prognostic biomarker in HFpEF. Baksi and Pennell in an editorial in Circulation: Cardiovascular Imaging, expresses optimism on the tremendous potential of T1 imaging to robustly measure diffuse fibrosis, guide therapy, and provide input to risk stratification models, which they feel will have far reaching impact on Cardiology in future.(Baksi and Pennell, 2013)

T2 Mapping in Heart Failure

Cardiac T2* magnetic resonance has emerged as an efficient tool to identify patients at high risk of heart failure and arrhythmia from myocardial siderosis in thalassemia major, establishing its superiority over serum ferritin and liver iron.(Kirk et al., 2009) Using cardiac T2* for the early identification and treatment of patients at risk has reduced the high burden of cardiac mortality in myocardial siderosis.(Modell et al., 2008)

CMR is the most accurate imaging modality for assessment of LV mass, systolic function, pericardium, and myocardial tissue characteristics as they relate to HFpEF.(Barison et al., 2022; Leong et al., 2010) In a recently published meta-analysis, looking at T2 times for various myocardial pathologies, the authors concluded that T2 times can reliably differentiate between healthy controls and patients with myocardial infarction, dilated cardiomyopathy, myocarditis, and heart transplant.(Snel et al., 2020) Global myocardial T2 relaxation time is significantly associated with quality of life, 6 min walking test, glomerular filtration rate and N-terminal pro brain natriuretic peptide (NT-proBNP) in these patients.(Doeblin et al., 2019) In specific sub-populations of HF like peripartum cardiomyopathy, persistence of LV dysfunction after 6 months follow-up can be predicted by longer myocardial T2 time

at baseline.(Liang et al., 2020)

It has been found that percentage of scar by LGE imaging independently predicted future events in cohorts of HFpEF. Murtagh et al used cardiac MRI derived LGE in the cardiac risk

stratification of patients with extracardiac sarcoidosis. LGE was present in 41 patients (20%). Among the 205 patients in the cohort, 12 patients (6%) died or had ventricular tachycardia (VT), 10 of these 12 patients (83%) were in the LGE+ group.(Murtagh et al., 2016) In another study, Pöyhönen et al evaluated the value of LGE imaging in patients suspected with non-ischaemic cardiomyopathy (NICM).(Pöyhönen et al., 2014) In their series with a mean LVEF of 52% (HFpEF), the event rate for MACE was 26% in patients with LGE+ versus 4% in patients without LGE (p = 0.041). The highest event rate was observed in patients with LGE volume of ≥17%. Thus, the presence of LGE while not essential in the cardiac MRI diagnosis of HFpEF appears to define the patients with a higher risk of major cardiovascular events, including death.

Heart failure with preserved ejection fraction in Asia

Heart failure with preserved ejection fraction (HFpEF) is a global public health problem. Unfortunately, little is known about HFpEF across Asia. To alleviate this lacunae, 1204 patients with HFpEF (left ventricular ejection fraction ≥50%) from 11 Asian regions, grouped as Northeast Asia (Hong Kong, Taiwan, China, Japan, Korea, n = 543), South Asia (India, n = 252), and Southeast Asia (Malaysia, Thailand, Singapore, Indonesia, Philippines, n = 409 were studied.(Weinreb et al., 2021)

It was found that Asian patients with HFpEF were relatively young (with more than a third under the age of 65 years) and lean (with only a fifth being obese) compared to those from Western populations; yet they carried a high co-morbidity burden (70% of patients had ≥2 co-morbidities). There were striking regional differences in types of co-morbidities, cardiac remodeling and outcomes of HFpEF across Asia: South Asians were the youngest and more often obese but had the lowest prevalence of AF despite the most concentric LV hypertrophy. Southeast Asian patients were only slightly older, yet had the highest prevalence of all co-morbidities (except AF), the most LVH and the worst outcomes. Northeast Asians were the oldest and had the most AF and eccentric LV hypertrophy. In terms of ethnicity, Indian and Malay patients with HFpEF were considerably younger than Chinese and Japanese/Korean patients. Despite their relative youth, Malay patients with HFpEF had very high rates of obesity, diabetes, CKD and anemia, and the worst outcomes among the ethnicities. These regional and ethnic differences have important implications for public health measures and global HFpEF trial design.

Compared to Western registries (GWTG-HF, SWEDE-HF, ADHERE-HF, and OPTIMIZE-HF) and studies performed in primarily Western populations (TOPCAT; I-PRESERVE and CHARM-Preserved), Asian patients with HFpEF are almost a decade younger compared to registries with Caucasian populations, while being of similar age to the TOPCAT and I-PRESERVE trials.(Alehagen et al., 2015; Cheng et al., 2014; Fonarow et al., 2007; Massie et al., 2008; Pitt et al., 2014; Tromp et al., 2019; Yancy et al., 2006) Despite their relatively young age, Asian patients with HFpEF had a relatively high prevalence of co-morbidities, particularly CKD, diabetes and hypertension. Overall, prevalence of CAD was relatively low compared to Caucasian populations. Obesity-related HFpEF is increasingly recognized as an important HFpEF phenotype.(Yusuf et al., 2003)

A recent publication from the INTER-CHF registry, which included a majority of HFrEF patients, showed that Chinese HF patients had better outcomes compared to Southeast Asian HF patients. However, Indian patients performed markedly worse in the INTER-CHF study, which can be explained by the inclusion of patients in more rural areas compared to ASIAN-HF as well as the fact that the INTER-CHF registry included a majority of HFrEF patients.(Shah et al., 2016)

Contemporary data from low- and middle-income countries are sparse regarding presentation, management, and outcomes of patients hospitalized with HF.(Dokainish et al., 2017) Harikrishnan and colleagues initiated a prospective hospital-based HF registry in the Trivandrum district of Kerala [Trivandrum Heart Failure Registry (THFR)], India in 2013.(Sivadasan Pillai and Ganapathi, 2013) The registry covered the Trivandrum city area (urban area, 215 km^2, population 957 000) and an adjacent suburban rural area. In comparison with other international registries, patients in our registry are relatively younger (*Table S3*). For example, the patients in the THFR are almost 8–10 years younger than the ADHERE registry, Korean registry, and the European Society of Cardiology registry.(Alehagen et al., 2015; Sivadasan Pillai and Ganapathi, 2013; Youn et al., 2012) The Kerala ACS and CREATE registries also show that Indians develop acute coronary events at a younger age.(Maggioni et al., 2013; Mohanan et al., 2013; Xavier et al., 2008)

There are minimal data on HFpEF patient in South East population with almost nil data on myocardial fibrosis assessment and its implication in HFpEF in Asians.

Our study aims to characterize the CMR findings and establish the utility of CMR in the evaluation of patients with HFpEF in a South East Asian population.

Materials and methods

Materials and methods

1. Hypothesis

Patient with HFpEF have subclinical or overt myocardial fibrosis manifested by increased T1 or LGE respectively.

2. Aim

To find out presence and extent of myocardial fibrosis and its clinical impact in patients with HFpEF.

3. Objectives:

- To document patient characteristics, including demographic profile, presenting symptoms and clinical signs in patients of HFpEF diagnosed with conventional echocardiography
- To study LV volume, mass, wall thickness, and EF by CMR in these patients
- To study LA volume and function by CMR in these patients
- To study RV function by CMR in these patients
- To evaluate the presence, and prognostic significance, of myocardial fibrosis in subjects with and without HFpEF, using Cardiac MRI
- To establish correlations of CMR findings with demographic characteristics and clinical profile of these patients.

4. Study design and study period

This study was a hospital record based ambi-directional observational study of all patients with HFpEF, who fulfilled the inclusion and exclusion criteria, and who underwent CMR between January 2018 and December 2022.

5. Selection of study population

The study population was selected from among the patients attending the Cardiology OPD or admitted to the Cardiology Department of Sree Chitra Tirunal Institute of Medical Science and Technology, Trivandrum, who fulfilled the following criteria:

Inclusion criteria:

A. Patients with clinical signs and/or symptoms of HF **and** BNP >35pg/mL and/or NT-proBNP>125 pg/mL **and** LVEF ≥50% on conventional echocardiography,**and** objective evidence of cardiac structural and/or functional abnormalities consistent with LV diastolic dysfunction/raised LV filling pressures, including raised NPs **and**,
B. **Either** attending the Cardiology OPD, SCTIMST, between September 2021 and December 2022, **or**,
C. Admitted to the Department of Cardiology, SCTIMST between September 2021 and December 2022, **or**,
D. Treated at SCTIMST, between January 2018 and August 2021

Parameters	Threshold
LVMI (gm/m2)	>95 female; >115 male
RWT	>0.42
LAVI (mL/m2)	>34 (SR), >40 (AF)
E/e' at rest	>9
NT Pro-BNP (pg/mL)	>125 (SR), >365 (AF)
PASP / TR velocity	>35 mmHg or / >2.8m/s

Exclusion criteria:

- Age < 18 years
- Severe valvular heart disease
- Congenital heart disease
- Pericardial diseases
- High output HF
- Significant CAD (Revascularized or indication for revascularisation)
- Hypertrophic cardiomyopathy or cardiac tumor or intra-cardiac mass
- With MRI incompatible implants
- With IV clips or metallic prosthesis
- Inability to lie flat in severe ADHF
- Claustrophobia, altered mental status
- eGFR <30mL/min
- Severe tachyarrhythmias
- Inability to hold breath
- Pregnant ladies
- Prisoners, and those unable to / unwilling to give informed consent

Control: 30 consecutive control patients who underwent CMRI as part of diagnostic evaluation for diagnosis other than HF and reported to be normal MRI were also taken for comparison.

6. Calculation of sample size

An approximate estimate of 0.5 HFpEF case per month was made at the beginning of the study and this lead to a projected sample size of 30 cases over the span of 5 years.

7. Carinal angle

Increased carinal angle was defined by carinal angle more than 75 degree.(Proschek and Vogl, 2015)

8. **Echocardiography:**

- LV end-diastolic diameter (LVEDD) and LV end-systolic diameter (LVESD) were measured in the Parasternal long axis view.(Lang et al., 2015)
- Ejection fraction (EF) was calculated by modified Simpson's biplane method.
- Diastolic function was standard ASE/ ESC guidelines.(Nagueh et al., 2016).
- Left atrial trial volume was calculated by the formula derived by(D1 × D2 × D3) × (0.523) formula where D2 is measured from the mitral annular plane to the back wall in apical 4-chamber view. D1 is the orthogonal short-axis dimension to D2. D3 is measured from the blood-tissue interface of the anterior and posterior walls in parasternal long axis view.(Jiamsripong et al., 2008)
- Left ventricular mass was calculated by both ASE and Th formula.(Devereux et al., 1986; Foppa et al., 2005; Teichholz et al., 1976)

2D Strain:

Longitudinal strain by speckle tracking echocardiography was obtained from three apical views (Apical 4 Chamber view, Apical 2 Chamber View, Apical 3 Chamber view) at a frame rate of > 50/s.

Global longitudinal strain (GLS) is defined as an average of peak longitudinal strain from an 18 left Ventricle (LV) Segments model.

Echocardiography, Strain echocardiography was done in the Philips EPIQ 7c model by a single operator.

9. CMR Protocol:

CMR examinations were done on 1.5 T Siemens (MAGNETOM Avanto, Siemens Healthcare, Erlangen, Germany) equipped with a 36-element dedicated cardiac array. The standard clinical CMR protocol consisted of scout images followed by functional assessment of the left ventricle using cine steady-state free precession techniques and post-contrast LGE images using phase-sensitive inversion recovery (PSIR) bSSFP sequence. Native T1 maps using the shortened modified Look-Locker inversion recovery (shMOLLI) technique with

collection of 6 region of interest in each basal, mid and apical segments (18-segment model) and inversion recovery times are separated by only one R-R interval, were acquired before contrast administration. The total acquisition time was around 40 minutes. All CMR images were stored in a picture archiving and communication system (PACS).

Cine images

Cine images were obtained using retrospective electrocardiographic gating in short axis, four-chamber, two-chamber, and three-chamber LV outflow tract imaging planes. A total of 25 cardiac phases were acquired during one R–R interval with temporal resolution <40 ms. A bright blood imaging technique using a bSSFP sequence was applied to obtain cine images. A short axis stack covered the heart from its base to apex, which allowed for the assessment of global and regional ventricular function, calculation of LV and RV volumes, ejection fraction, and LV mass.

Native T1

Native T1 sequence was obtained using shMOLLI sequence before intravenous administration of contrast in three short-axis imaging planes, one each at the base, mid-ventricle, and apex of the LV.

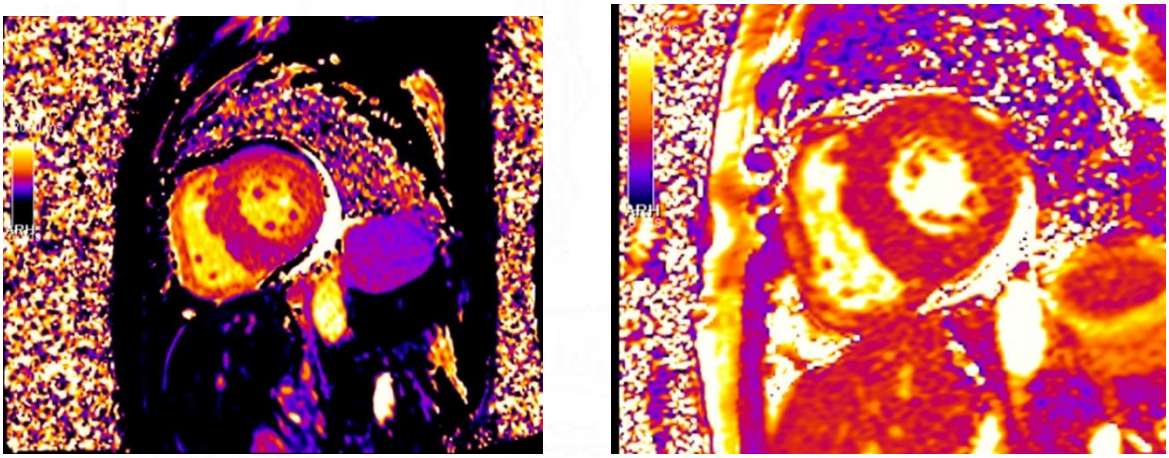


Fig B: Representative image showing T1 (left) and T2 (right) colour mapping

LGE sequence:

LGE images were obtained 10 minutes after administrating intravenous Gadolinium-based contrast medium (Gadotrast, Gadoterate Meglumine, Unique pharmaceuticals, India)

intravenously at 0.1 mmol/kg body weight. Breath-hold segmented ECG gated PSIR bSSFP sequence performed in the same orientation as the cine images. The inversion time was adjusted to completely null normal myocardium (typically 250-400 ms).

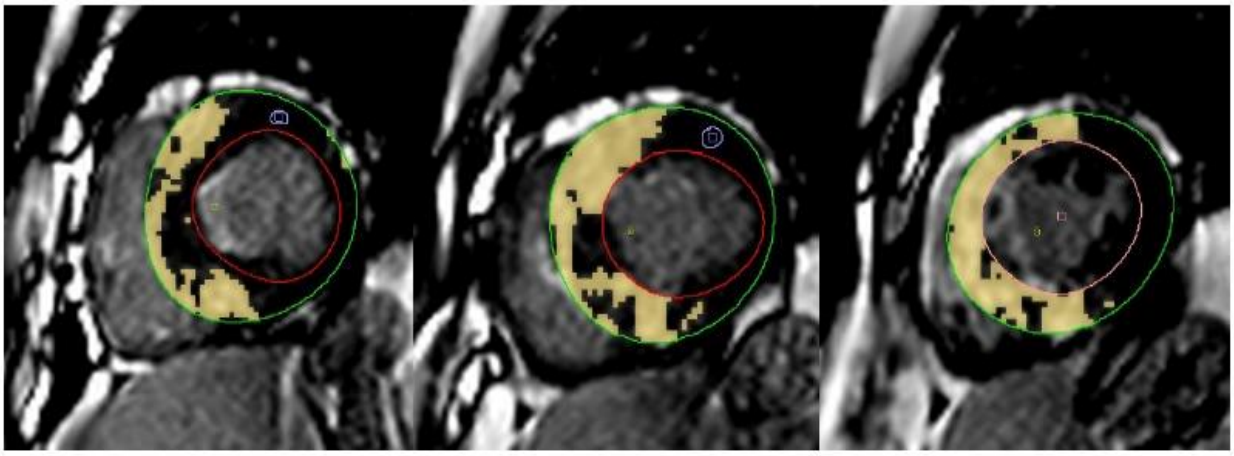


Fig C: LGE quantification in cvi42 software – yellow highlighted areas represents LGE

Image analysis

For the study, CMR images were retrieved from PACS, anonymized, and stored separately in numbered folders. These images were post-processed and analysed by a reader with 3 years of experience in interpreting CMR studies. CMR data were analysed using commercially available post-processing software. Absolute and indexed LV volumes, myocardial mass, LV and RV ejection fractions, native T1, and extent of myocardial LGE, were measured using cvi42 Version 5.13.7 (Circle Cardiovascular Imaging, Calgary, Alberta, Canada) by a single experienced reader (3 years of CMR experience). Cine images were used to measure LV ejection fraction and volumes by tracing the endocardial and epicardial boundaries at the end-diastole and end-systole. Ejection fraction and myocardial mass were obtained using the semi-automated technique. Papillary muscles were excluded from the calculation of myocardial mass. The wall thickness of 18 LV myocardial segments was measured and the maximum wall thickness and well as the segment involved were noted. The left atrial anteroposterior diameter (LAD-AP) was taken as the maximum distance from the posterior

wall of the left atrium to the mitral valve during the cardiac cycle, measured in a four-chamber view. Epicardial and endocardial borders contoured long axis extent, and RV insertion points were selected, after which the global and segmental native T1 values were automatically computed by the software.

LGE images were reviewed and the presence or absence of scar in the LV was noted. Further, the percentage extent of LGE in the LV as a percent of total LV mass was calculated using the mean + 5SD method. A user-defined free hand region of interest was drawn within normal nulled remote myocardium in the short axis stack of LGE PSIR images after contouring the epicardial and endocardial borders to obtain software-generated percentage extent of LGE.

All areas that were identified as enhancement by the software were cross-verified by the reader to ensure the exclusion of inversion time artefact or contamination by blood pool or pericardial fat. These were manually excluded by contour adjustment or the exclusion tool available in the software. The presence and absence of LGE in each segment were also recorded.

10. Data tabulation

Relevant clinical and Echocardiography findings were incorporated in the pre-designed Case Record Form (Annexure 1). This data were transferred to the Master Chart (Annexure 2) for statistical analysis

11. Statistical analysis

Statistical analyses were performed using STATA version 14 (Stata Corporation, College Station, Texas, USA) software. All tests were two-sided, and a $P < 0.05$ was considered statistically significant. Continuous variables were expressed as mean ± 2 SD if normally distributed or as medians (25th and 75th percentiles) if not normally distributed. Categorical variables were expressed as counts and percentages. Comparisons between groups were made by ANOVA, chi-square test, paired/ unpaired sample *t* test wherever appropriate for continuous variables with normal distribution, Wilcoxon signed rank test for continuous

variables with nonnormal distribution, and Fisher exact test for categorical variables. Logistic regression was performed to determine predictors of abnormal diffuse HFpEF (above or below 95% confidence intervals in controls). For this purpose, after univariate comparison of the two groups, parameters with a $P < 0.20$ were proposed for inclusion in the multiple logistic regression analysis with a backward selection procedure. Correlation of variables was expressed by Pearson correlation coefficient. Bias and precision between techniques were evaluated using Bland-Altman plots.

Results and analysis

Results and analysis

The mean (±SD) age of the HFpEF population was 63 ± 8 years with that in the control population being 61 ± 6 years with no significant statistical difference between the two groups. There was a female predominance in both groups with 87% female in the HFpEF group. There was no difference in height or body surface area in both the groups. In keeping with the observations of the south-Asian consensus guidelines, 93% of the study population in case group were obese, in contrast to 57% in the control group, yielding a significant statistical difference in the mean BMI of the cases and controls (p <0.001) **(Table 6).**

	Cases (N = 30)	Controls (N = 30)	p
Age (mean ±SD) in Years	63 ± 8	61 ± 6	0.123
Female (%)	26 (87)	24 (80)	0.731
Ht (cm) (mean ±SD)	150 ± 7	153 ± 8	0.105
BMI (kg/m2) (mean ±SD)	29.5 ± 4.8	25.8 ± 2.4	<0.001
BSA (m2) (mean ±SD)	1.62 ± 0.18	1.58 ± 0.12	0.324

Table 6: Demographic profile of study population (n = 60)

40% of the cases were diabetic as compared to 10% in control group which was statistically significant (p <0.001). Systemic hypertension and dyslipidemia were more prevalent in cases (87% and 47% respectively) as compared to controls with p <0.001. History of chronic obstructive pulmonary disease, and coronary artery disease were significantly higher in cases compared to controls (p = 0.005, p = 0.024, respectively). There was no statistical difference observed in terms of history of obstructive sleep apnoea, family history of coronary artery disease or prior history of COVID-19 infection **(Table 7).**

	Cases (%) (N = 30)	Controls (%) (N = 30)	p
DM	12 (40)	3 (10)	<0.001
HTN	26 (87)	4 (13)	<0.001
Hypothyroid	2 (7)	0	0.492
COPD	8 (27)	0	0.005
CAD	6 (20)	0	0.024
Dyslipidemia	14 (47)	0	<0.001
OSA	4 (13)	0	0.112
F/h CAD	2 (7)	0	0.492
H/O COVID	4 (13)	0	0.112
WHO guidelines			
No obesity	4 (13)	13 (43)	<0.001
Overweight	16 (53)	17 (57)	
Obese	10 (33)	0	
South-Asian Guidelines			
No	2 (7)	3 (10)	<0.001
Overweight	0	10 (33)	
Obese	28 (93)	17 (57)	

Table 7: Co-morbidities and personal history of study population

All patients had dyspnoea with NYHA functional class II or more and 20% presented with history of paroxysmal nocturnal dyspnoea. 33% had chronic cough and 40% had history of palpitations. Only 1 patient (3%) had anasarca and there was no history of syncope in either limb of the study population **(Table 8).**

	Cases (N = 30)	Controls (N = 30)	p
SOB	30 (100)	2 (7)	<0.001
PND	6 (20)	0	0.024
Cough	10 (33)	0	0.001
Expectoration	0	0	N/A
Anasarca	1 (3)	0	1.000
Oliguria	0	0	N/A
Angina	6 (20)	0	0.024
Palpitation	12 (40)	3 (10)	<0.001
Syncope	0	0	N/A

Table 8: Clinical presentation in HFpEF (n = 30)

There was significant difference in respiratory rate at presentation between both groups (17 vs 13 per minute, p <0.001) and in the baseline oxygen saturation at presentation (96% vs 99%, p <0.001). 33% of the cases had bilateral pitting pedal oedema with no patient in control group having the same clinical feature (p <0.001) **(Table 9).**

	Cases (N = 30)	Controls (N = 30)	p
Pulse rate, bpm	80 ± 20	77 ± 9	0.490
Respiratory rate (per min)	17 ± 6	13 ± 1	<0.001
Saturation @ RA (%)	96.4 ± 4.7	98.8 ± 0.9	0.001
Murmur, %	6 (20)	0	0.024
Pedal edema, %	10 (33)	0	0.001

Table 9: Clinical findings of study population (n = 30)

The H2FPEF and the HFA – PEFF scores were calculated for out study population. The mean H2FPEF score was 5 in our case population. Coming to the more exhaustive and inclusive HFA – PEFF score which incorporates detailed echocardiography and biomarker estimations results, the mean HFA-PEFF score was 5.2, with a median score of 5.2 **(Figure 1).**

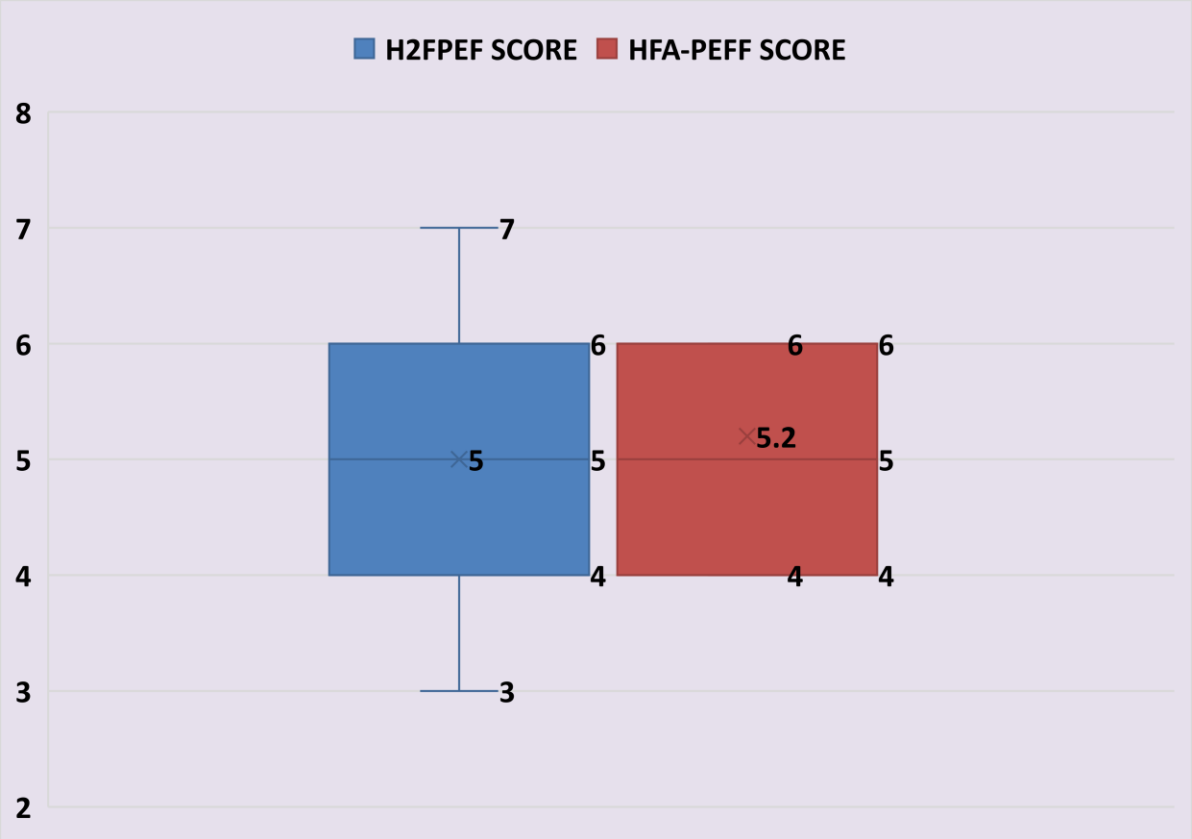


Figure 1: HFpEF scoring system application in study population

Among the 30 patients included to represent the HFpEF arm, 87% were on ACE inhibitors and 87% were on diuretics, with all of the latter being on loop diuretics. 53% of the cases were on mineralocorticoid receptor antagonists. Other antihypertensive drugs were also represented in the study cohort like beta-blockers (47%), calcium channel blockers (27%), and Hydralazine (3%). Only 27% patients were on SGLT2-inhibitors **(Figure 2).**

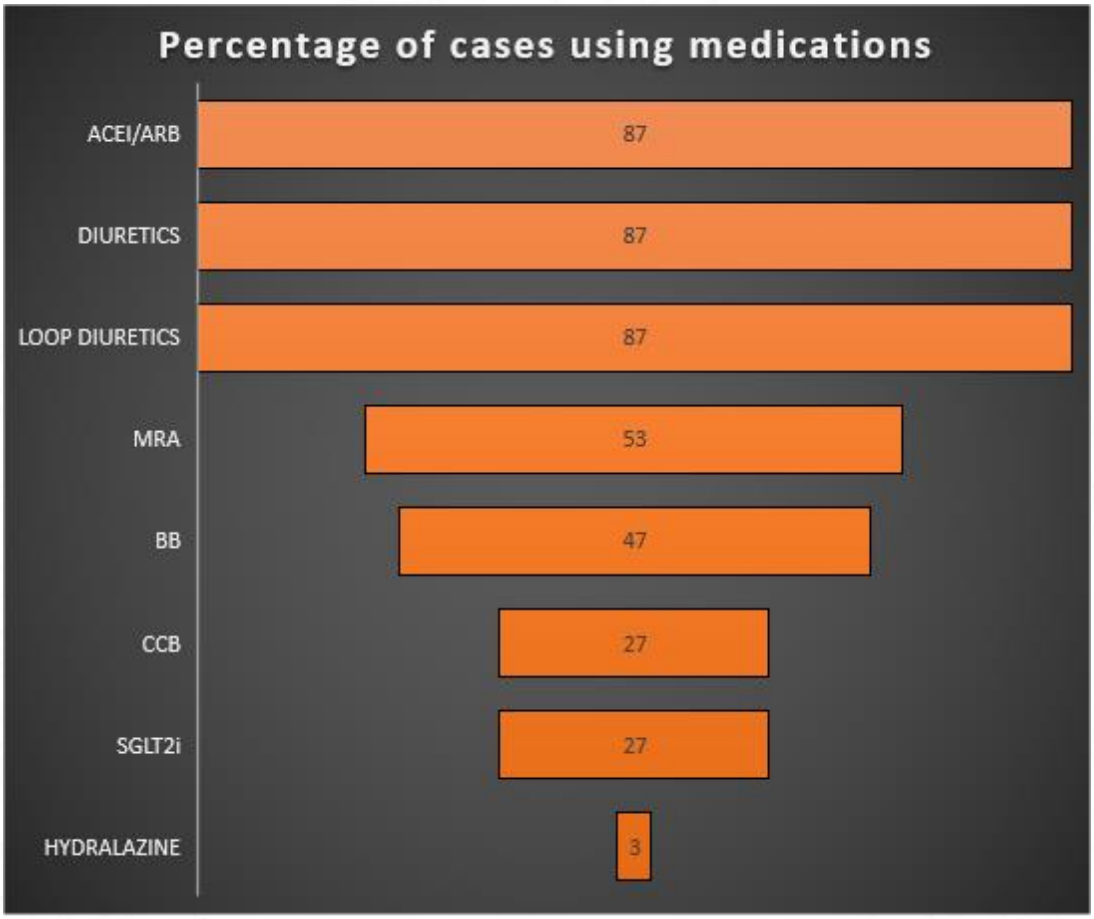


Figure 2: Antihypertensive drugs used in the study population

Coming to basic laboratory parameters, the Hemoglobin, serum creatinine and serum thyroid stimulating hormone (TSH) values were normal and comparable in both the groups **(Table 10).**

	Cases (N = 30)	Controls (N = 30)	p
Hb g/dL (mean ±SD)	13.1 ± 1.6	13.2 ± 0.5	0.803
Creatinine mg/dL (mean ±SD)	1.01 ± 0.26	0.89 ± 0.12	0.056
TSH mIU /L (mean ±SD)	2.9 ± 1.0	3.1 ± 0.9	0.518

Table 10: Lab parameters of study population

Focusing on the ECG findings, 80% of the cases were in sinus rhythm and the rest were in atrial fibrillation, while all members of the control population were in sinus rhythm. Among the cases, 27% had electrocardiographic features of left atrial enlargement and 13% had left ventricular hypertrophy by standard electrographic criteria for left ventricular hypertrophy. QRS axis was slight leftward in the study group as compared to the control population (27 degrees vs 44 degrees, *p=0.026*). QRS duration (88ms vs 70ms, *p=0.031*) and QTc (404ms vs 393ms, *p=0.002*) were significantly prolonged in cases compared to controls. PR interval was similar in both the groups **(Table 11).**

	Cases (N = 30)	Controls (N = 30)	p
Sinus rhythm, %	24 (80)	30 (100)	0.024
LAE (n=24), %	8 (27)	0	<0.001
PR duration (n=24) mS	158 ± 23	151 ± 13	0.199
QRS Axis, degree	27 ± 37	44 ± 21	0.026
QRS duration , mS	88 ± 31	70 ± 4	0.002
QTC, mS	404 ± 22	393 ± 16	0.031
LVH, %	4 (13)	0	0.112
ST T changes , %	16 (53)	0	<0.001

Table 11: ECG findings in the study population

Cardiac enlargement was present in 73% of the cases with mean cardio-thoracic ratio being 57% in cases compared to 47% in control, which was statistically significant *(p <0.001)*. Left atrial enlargement (Carinal angle >75 degree) was found in 60% of the cases compared to none in control. 93% of the cases had chest X-ray evidence of pulmonary venous hypertension with grade I pulmonary venous hypertension being the most prevalent (60%). Non-specific lung field abnormalities (fibrosis, minimal bronchiectasis) were present in 13% of the cases **(Figure 3, 4, Table 12).**

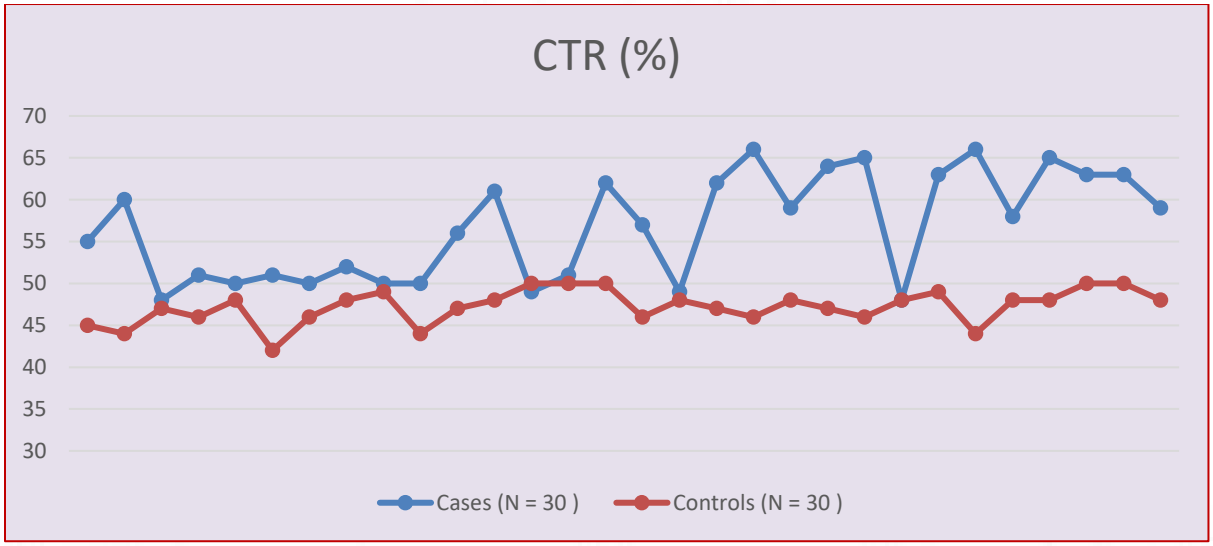


Figure 3: Cardiothoracic ratio among cases and control

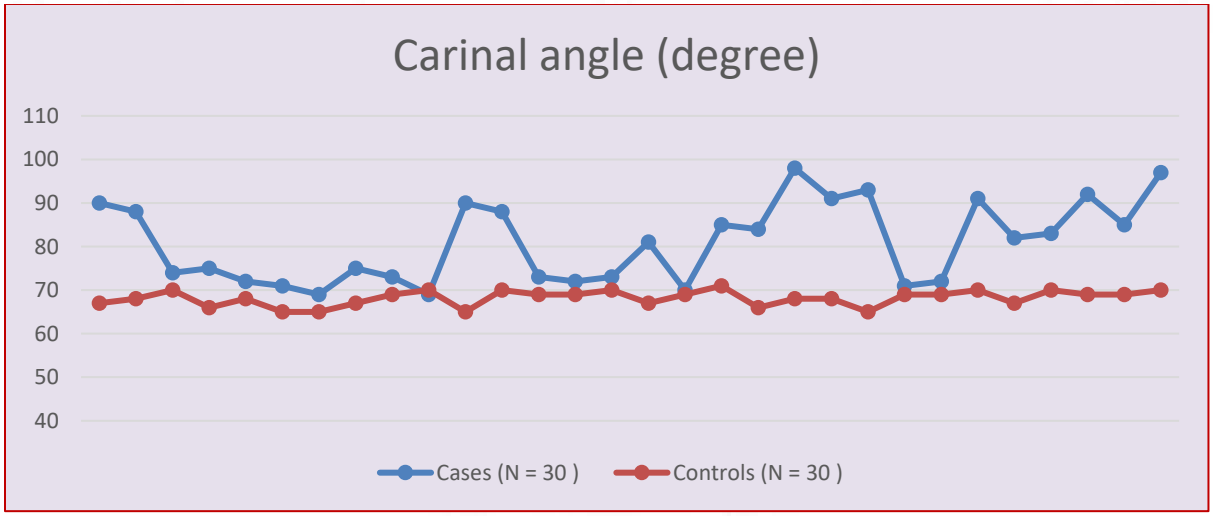


Figure 4: Carinal angle among cases and control

	Cases (%) (N = 30)	Controls (%) (N = 30)	p
CE	22 (73)	0	<0.001
CTR, %	57 ± 6	47 ± 2	<0.001
LAE	18 (60)	0	<0.001
Carinal angle, degree	81 ± 9	68 ± 2	<0.001
PVH Grade			
0	2 (7)	30 (100)	<0.001
1	18 (60)	0	
2	5 (17)	0	
3	5 (17)	0	
PAH	20 (67)	0	<0.001
Lung field abnormalities	4 (13)	0	0.112

Table 12: CXR findings in study population

53% of the cases had grade II left ventricular diastolic dysfunction, whereas grade I and III LVH constituted 34% and 13% respectively **(Figure 5).**

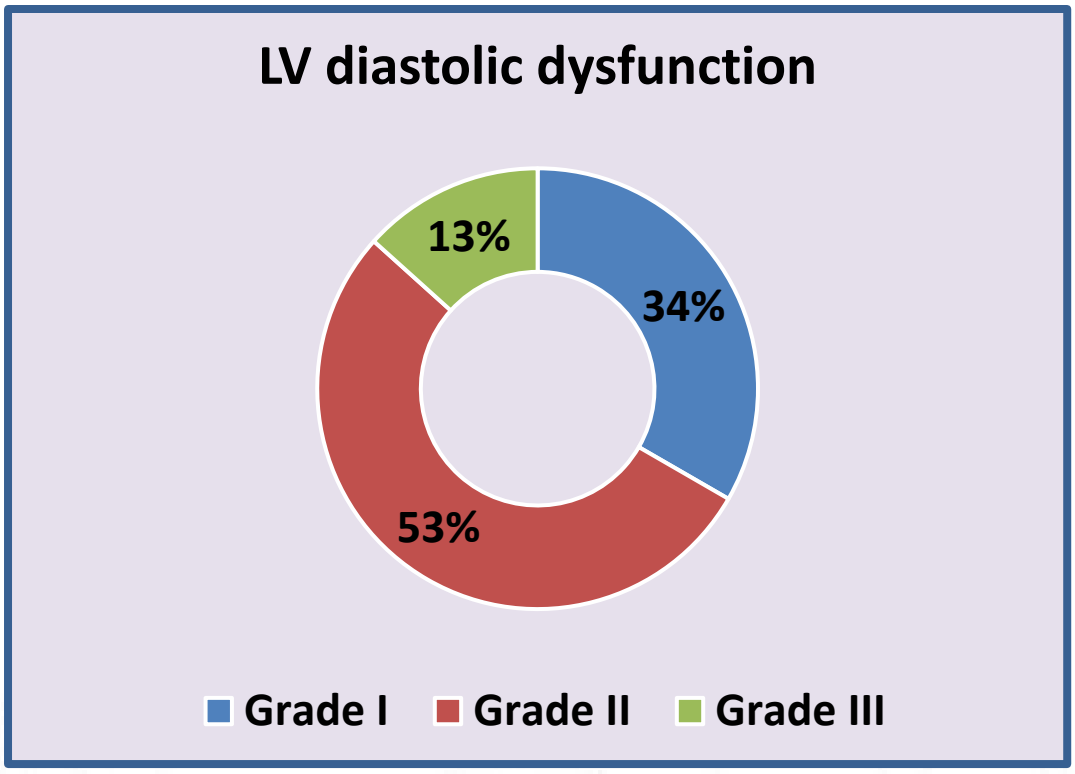


Figure 5: Distribution of degrees of LVH in the study population

Echocardiographic parameters were analyzed across cases and controls. 53% of the cases as compared to none in control group had concentric left ventricular hypertrophy as per ASE guidelines *(p <0.001)*. 7% had concentric remodeling and 20% had eccentric hypertrophy. Septal and posterior wall thickness more than or equal to 11mm was present in 70% of the cases. Mean inter-ventricular septal thickness in diastole (mean ± SD; 12.0 ± 2.2) and systole (mean ± SD; 14.2 ± 2.1) were significantly higher in case compared to control group in diastole and systole. Mean left ventricular posterior wall thickness in diastole (mean ± SD; 11.1 ± 1.9) and systole (mean ± SD; 13.5 ± 2.0) were significantly higher in cases as compared to controls. Left ventricular mass index was significantly higher in cases both by Teichholz (mean ± SD; 108 ± 23 vs 70 ± 12) and ASE formula (mean ± SD; 120 ± 29 vs 72 ± 13) **(Figure 6, Table 13).**

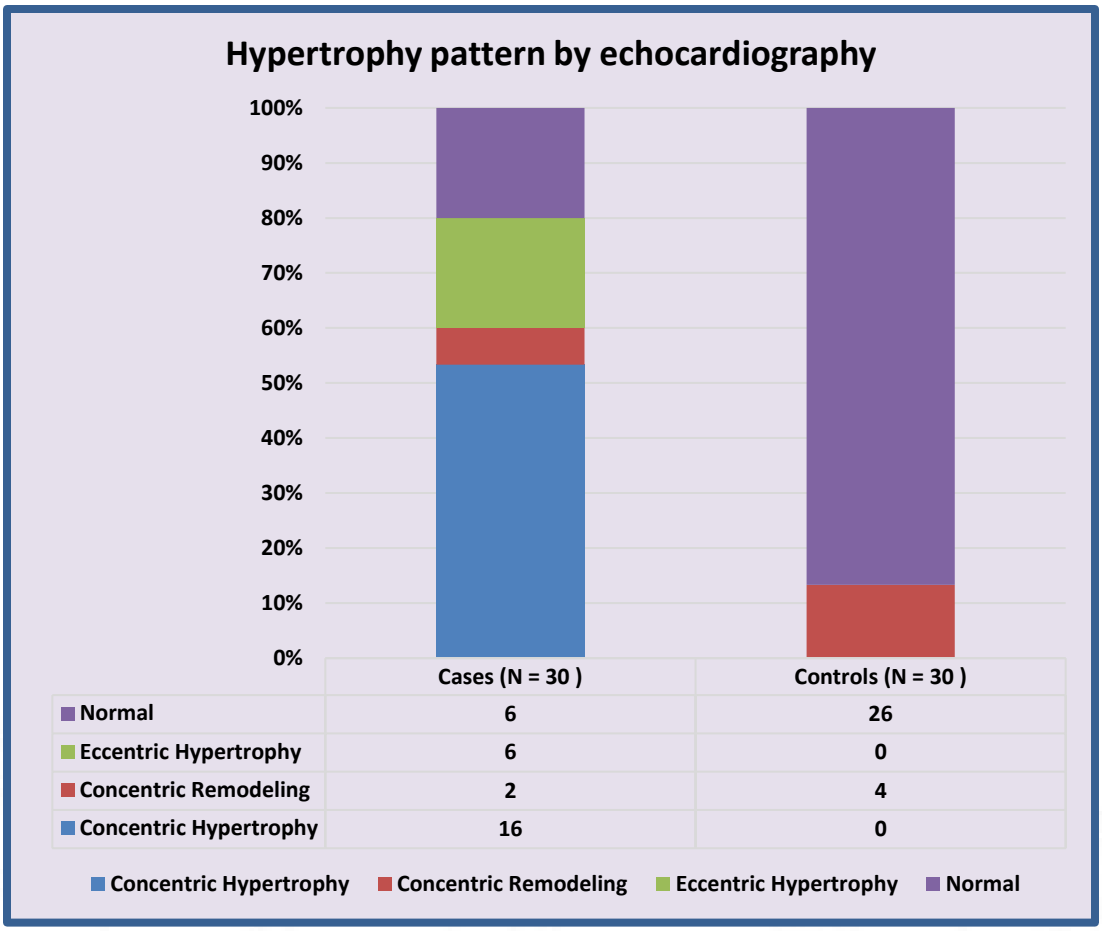


Figure 6: Echocardiographic parameters, 1

	Cases (N = 30)	Controls (N = 30)	p
LVIDD, mm	45.5 ± 3.6	42.4 ± 2.9	<0.001
LVIDS, mm	28.4 ± 3.2	25.3 ± 2.9	<0.001
IVS D, mm	12.0 ± 2.2	8.7 ± 0.9	<0.001
IVS S, mm	14.2 ± 2.1	10.9 ± 0.9	<0.001
PW D, mm	11.1 ± 1.9	8.4 ± 0.5	<0.001
PW S, mm	13.5 ± 2.0	10.7 ± 0.7	<0.001
LV mass (ASE), gm	191 ± 37	113 ± 19	<0.001
LV mass index (ASE), gm/m^2	120 ± 29	72 ± 13	<0.001
LV mass (Th), gm	172 ± 28	110 ± 16	<0.001
LV mass index (Th), gm/m^2	108 ± 23	70 ± 12	<0.001
RWT	0.49 ± 0.12	0.40 ± 0.03	<0.001
Hypertrophy (%)			
Concentric Hypertrophy	16 (53)	0	<0.001
Concentric Remodeling	2 (7)	4 (13)	
Eccentric Hypertrophy	6 (20)	0	
Normal	6 (20)	26 (87)	
LVH on Echo	21 (70)	0	<0.001

Table 13: Echocardiographic parameters, 1

Further echocardiographic findings revealed that the Right ventricular internal diameter (RVID) was significantly higher in cases as compared to controls (mean ± SD; 23.5 ± 3.5 vs 19.8 ± 2.4, $p < 0.001$). While the left ventricular ejection fraction was similar in both the groups, the Left atrial volume index was significantly higher in cases (mean ± SD; 31.5 ± 9.6 vs 18.1 ± 3.6, $p < 0.001$). No statistical differences were found in terms of fractional left ventricular change or regional wall motion abnormality **(Table 14).**

	Cases (N = 30)	Controls (N = 30)	p
RVID, mm	23.5 ± 3.5	19.8 ± 2.4	<0.001
EF, %	66 ± 7	68 ± 7	0.246
FC, %	38 ± 6	40 ± 6	0.073
LA PLAX, mm	41.3 ±4.7	33.1 ± 2.4	<0.010
LA A4C L, mm	55.8 ± 6.8	49.3 ± 4.4	<0.001
LA A4C W, mm	41.2 ± 5.8	33.2 ± 3.04	<0.001
LAV, mL	50.7 ± 16.2	28.6 ± 5.2	<0.001
LAV I , mL/m2	31.5 ± 9.6	18.1 ± 3.6	<0.001
Aorta, mm	29.4 + 3.8	28.0 ± 2.7	0.095
RWMA, %	2 (7)	0	0.492

Table 14: Echocardiographic parameters, 2

The Mitral E velocity deceleration time was significantly lower in cases as compared to controls (mean ± SD; 154 ± 32 vs 207 ± 14, $p < 0.010$). Diastolic mitral inflow L velocity of more than 40cm/sec was present in 20% of the cases and none in control group. Lateral and medial mitral annular velocity in tissue Doppler imaging was lower in case group compared to control. Average E/e' was significantly higher in cases than in the control subpopulation (mean ± SD; 17.5 ± 7.2 vs 7.7 ± 1, $p < 0.010$) **(Table 15).**

	Cases (N = 30)	Controls (N = 30)	p
MV E, m/s	1.07 ± 0.33	0.90 ± 0.16	0.010
MV A, m/s	0.90 ± 0.24	0.71 ± 0.12	<0.001
EDT (mS)	154 ± 32	207 ± 14	<0.001
L wave (%)	6 (20)	0	0.024
LAT E', cm/s	7.6 ± 2.3	14.1 ± 2.3	<0.001
LAT E/E'	15.6 ± 7.2	6.5 ± 1.5	<0.001
MED E', cm/s	5.8 ± 1.3	10.4 ± 1.6	<0.001
MED E/E'	19.4 ± 7.5	8.9 ± 2.1	<0.001
AVG E/E'	17.5 ± 7.2	7.7 ± 1.7	<0.001
LAT A', cm/s	8.9 ± 3.2	11.0 ± 1.5	0.002
MED A', cm/s	8.6 ± 2.9	8.2 ± 1.6	0.542

Table 15: Echocardiographic parameters, 3

The mean tricuspid regurgitation gradient in the cases with HFpEF was 35mmHg compared to 15mmHg in the control group. There were no differences in terms of other milder forms of valvular lesions. 33% patient had mild pericardial effusion on echocardiogram whereas no pericardial effusion was noted in control group. Global longitudinal strain was significantly reduced in case group (at least one segment having less than -17) compared to control (33% vs 0%, *P<0.001*) **(Table 16).**

	Cases (N = 30)	Controls (N = 30)	p
TR Gradient, mmHg	35 ± 8	15 ± 4	<0.001
TAPSE, mm	20 ± 2	21 ± 1.8	0.038
AOV, m/s	1.33 ± 0.30	1.11 ± 0.16	<0.001
PV, m/s	1.03 ± 0.16	0.99 ± 0.11	0.317
MR, %	1.80 ± 0.76	0.20 ± 0.05	<0.001
PE, %	10 (33)	0	<0.001
AR, %	4 (13)	0	0.112
AS, %	2 (7)	0	0.492
GLS abnormality, %	20 (67)	0	<0.001

Table 16: Echocardiography findings, 4

CMRI data

Left ventricular internal diameter in both systole and diastole were comparable in both the group (p = 0.443 and 0.098, respectively). However interventricular septal thickness in diastole (mean ± SD; 9.9 ± 2.6 vs 8.0 ± 2.0mm, p = 0.004) and systole (mean ± SD; 14.8 ± 2.3 vs 2.1 ± 1.9mm, p < 0.001) were significantly higher in case group. Similarly left ventricular posterior wall thickness were higher in cases in both diastole (mean ± SD; 8.7 ± 2.5 vs 6.1 ± 1.3mm, p < 0.001) and systole (mean ± SD; 14.6 ± 3.2 vs 11.8 ± 2.7mm, p < 0.001). Left atrial volume index on MRI was significantly higher in case group (mean ± SD; 34.1 ± 9.4 vs 22.7 ± 5.9ml/m^2, p < 0.001) as compared to controls **(Figure 7, Table 17).**

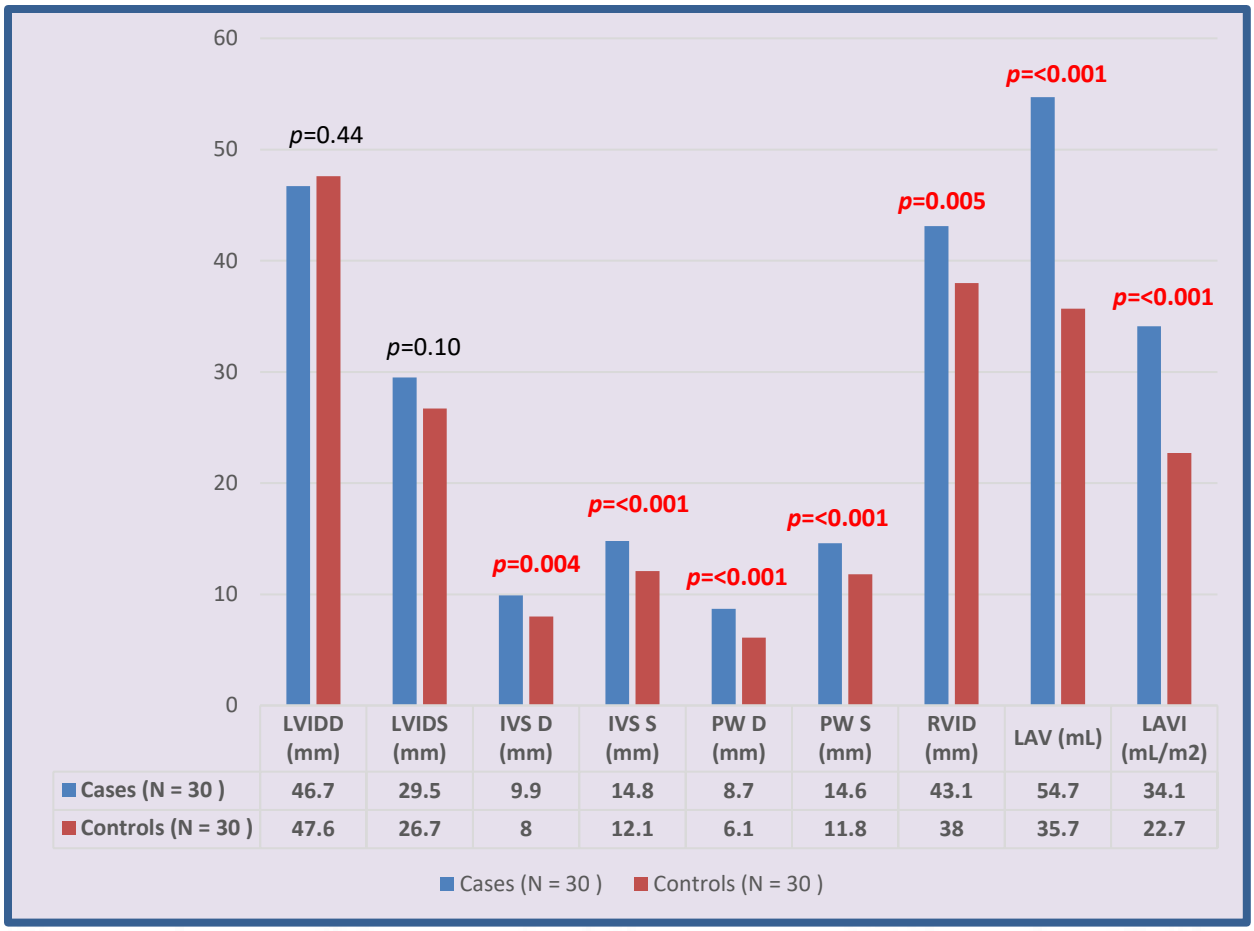


Figure 7: CMRI parameters, 1

	Cases (N = 30)	Controls (N = 30)	p
LVIDD, mm	46.7 ± 4.0	47.6 ± 5.3	0.443
LVIDS, mm	29.5 ± 5.9	26.7 ± 6.8	0.098
IVS D, mm	9.9 ± 2.6	8.0 ± 2.0	0.004
IVS S, mm	14.8 ± 2.3	12.1 ± 1.9	<0.001
PW D, mm	8.7 ± 2.5	6.1 ± 1.3	<0.001
PW S, mm	14.6 ± 3.2	11.8 ± 2.7	<0.001
RVID, mm	43.1 ± 4.1	38.0 ± 3.5	0.005
LV mass, gm	91 ± 28	71 ± 15	0.001
LV mass index, gm/m^2	57 ± 20	45 ± 10	0.005
LA 4C L, mm	48.3 ± 5.0	43.7 ± 4.6	<0.001
LA 4C W, mm	47.8 ± 5.4	39.6 ± 5.3	<0.001
LA, mm	44.7 ± 5.3	39.1 ± 4.5	<0.001
LAV, mL	54.7 ± 14.8	35.7 ± 8.4	<0.001
LAVI, mL/m2	34.1 ± 9.4	22.7 ± 5.9	<0.001

Table 17: CMRI parameters, 1

Left ventricular mass index was significantly higher in cases as compared to controls, (mean ± SD; 57 ± 20 vs 45 ± 10 gm/m^2, p = 0.005) as were the left ventricular end diastolic volume index (LVEDVi) (mean ± SD; 66 ± 13 vs 54 ± 10 mL/m^2, p < 0.001), Left ventricular end systolic volume index (LVESVi) (mean ± SD; 43 ± 9 vs 35 ± 6 gm/m^2, p = 0.016). MRI derived left ventricular ejection fraction was similar in both the groups (mean ± SD; 66 ± 6 vs 66 ± 8 %, p = 0.67) **(Figure 8, Table 18).**

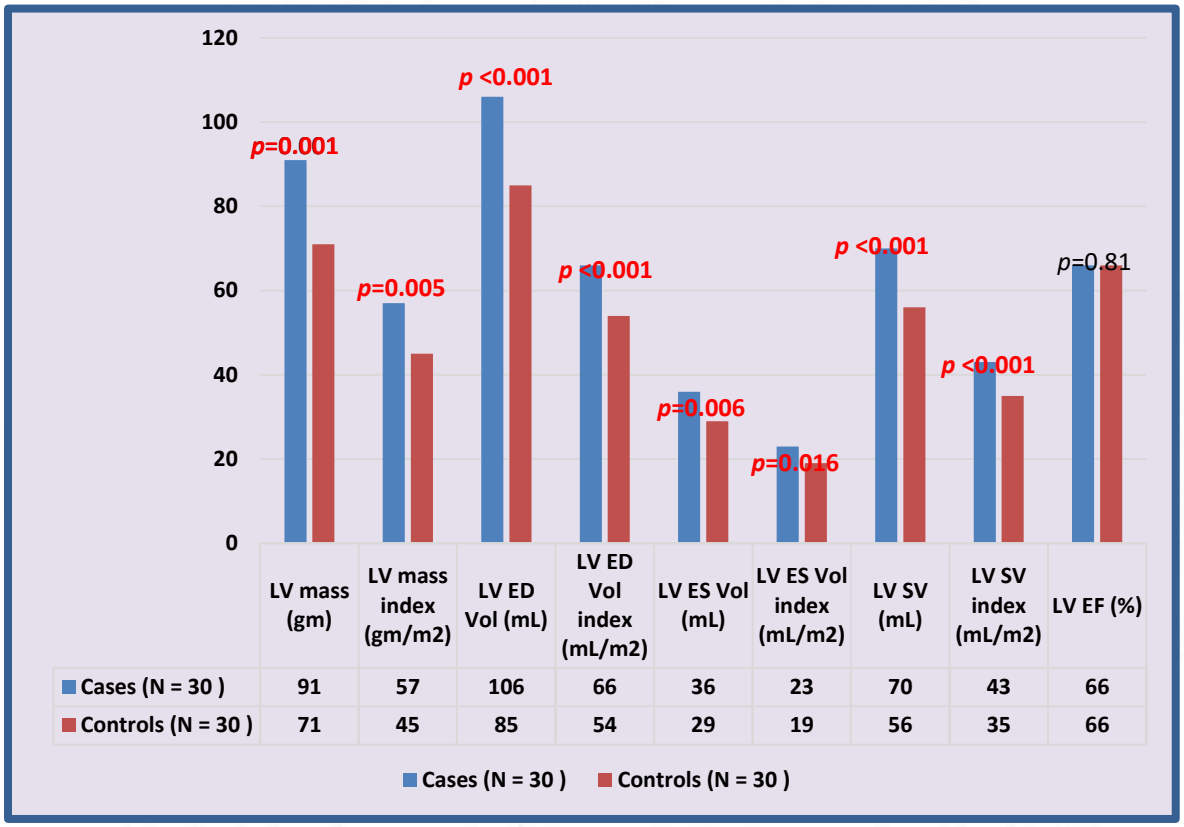


Figure 8: CMRI parameters, 2

	Cases (N = 30)	Controls (N = 30)	p
LV ED Vol, mL	106 ± 19	85 ± 15	<0.001
LV ED Vol index, mL/m2	66 ± 13	54 ± 10	<0.001
LV ES Vol, mL	36 ± 9	29 ± 10	0.006
LV ES Vol index, mL/m2	23 ± 6	19 ± 7	0.016
LV SV, mL	70 ±15	56 ±9	<0.001
LV SV index, mL/m2	43 ± 9	35 ± 6	<0.001
LV CO, L/min	4.71 ± 1.13	4.86 ± 0.87	0.559
LV CO index, L/min/m	2.93 ± 0.73	3.09 ± 0.58	0.350
LV EF, %	66 ± 6	66 ±8	0.809
RV ED Vol, mL	104 ± 24	124 ± 27	0.004
RV ED Vol index, mL/m2	64 ± 11	79 ± 18	<0.001
RV ES Vol, mL	46 ± 14	48 ± 14	0.667
RV ES Vol index, mL/m2	29 ± 7	30 ± 9	0.364
RV SV, mL	59 ± 17	76 ± 20	<0.001
RV SV index, mL/m2	36 ± 9	48 ± 13	<0.001
RV CO, L/min	4.18 ± 1.35	4.89 ±0.91	0.020
RV CO index, L/min/m^2	2.56 ± 0.75	3.11 ± 0.62	0.003
RV EF, %	56 ± 10	61 ± 8	0.03
LGE, %	8 (27)	0	0.005

Table 18: CMRI parameters, 2

Left ventricular cardiac output index were similar in both the groups (mean ± SD; 2.93 ± 0.73 vs 3.09 ± 0.58 L/min, p = 0.35), whereas right ventricular cardiac output was lower in case group when compared to control (mean ± SD; 2.56 ± 0.75 vs 3.11 ± 0.62 L/min, p = 0.003).

Right ventricular end diastolic volume index was lower in case as compared to control group (mean ± SD; 64 ± 11 vs 79 ± 18 mL/m^2, p <0.001), as were the right ventricular stroke volume

index (mean ± SD; 36 ± 9 vs 48 ± 13 mL/m^2, p <0.001) and right ventricular ejection fraction (mean ± SD; 56 ± 10 vs 61 ± 8%, p =0.03) **(Figures 9, 10, Table 19)**.

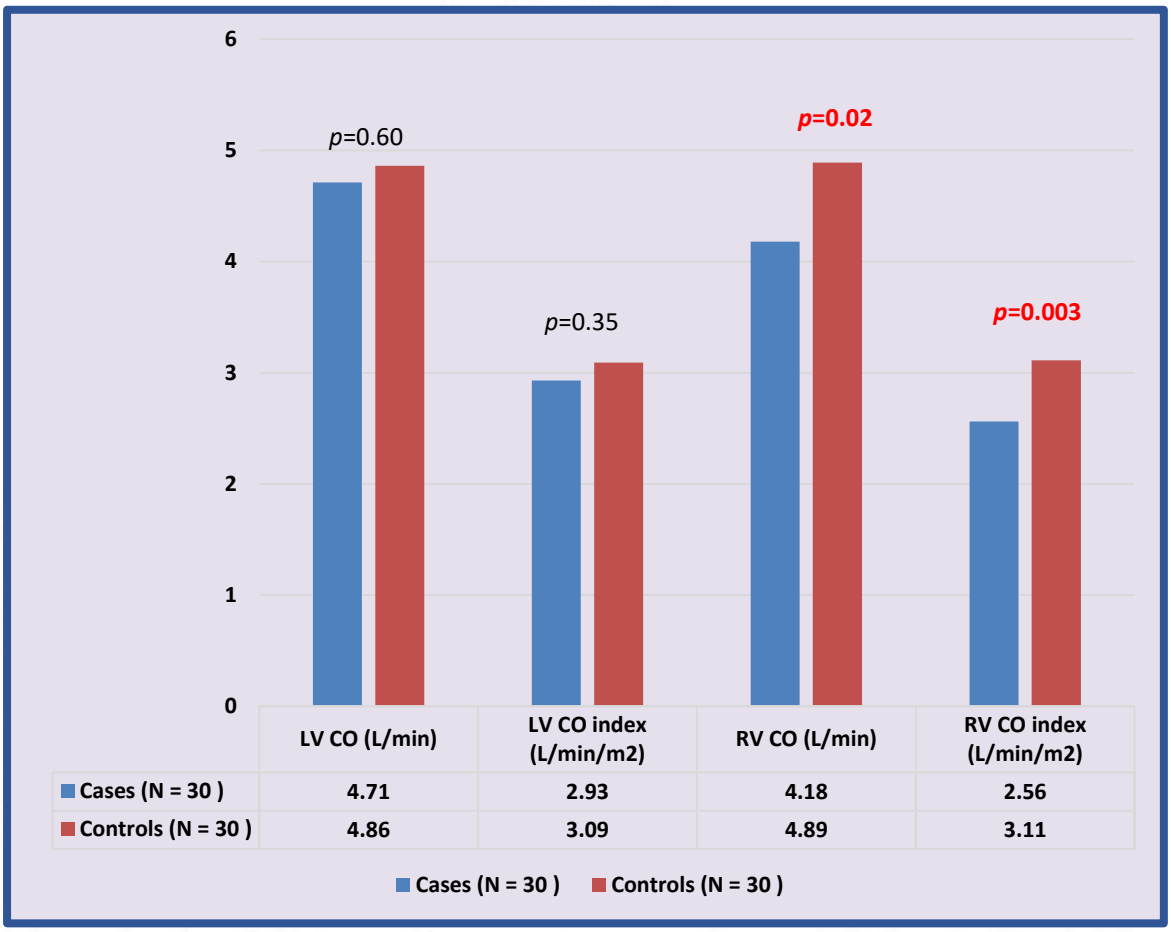


Figure 9: CMRI parameters, 3

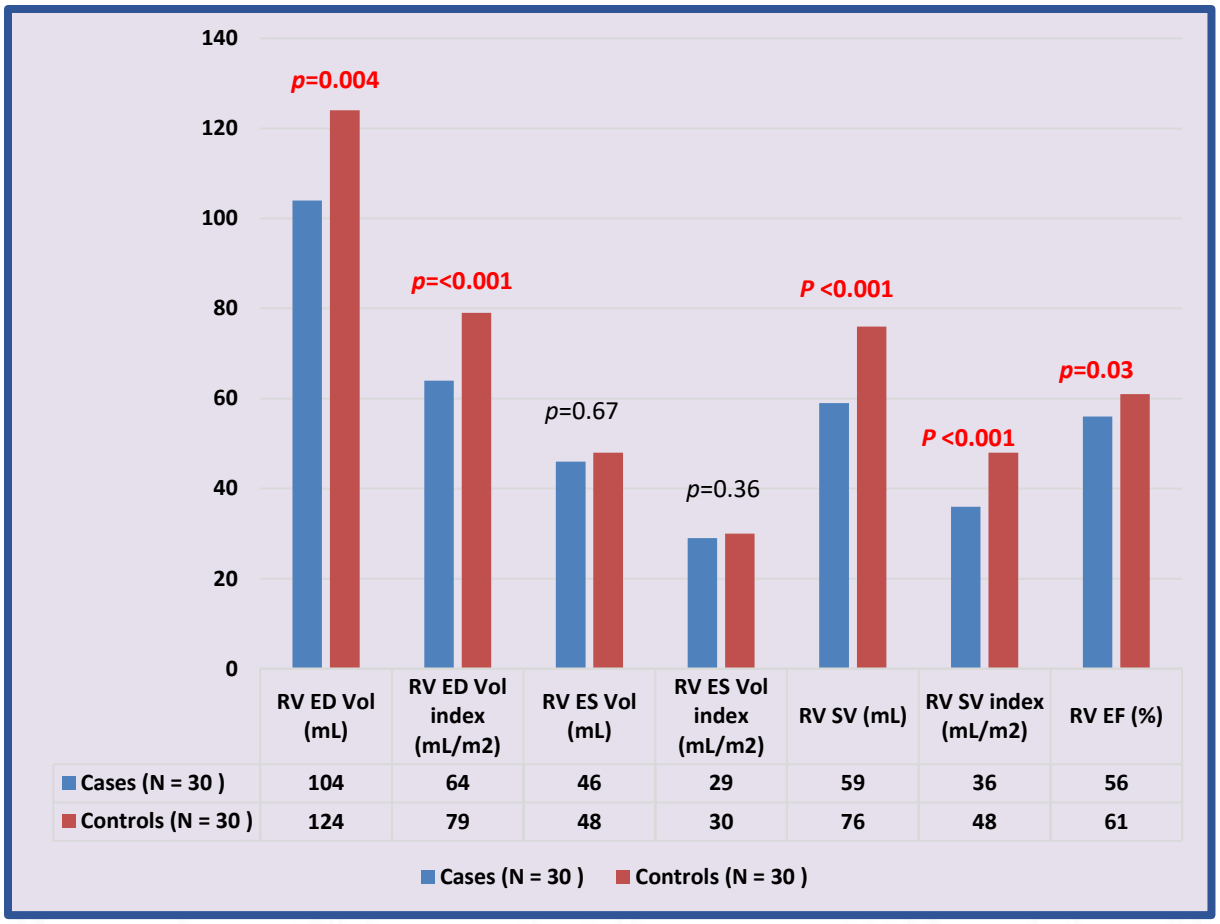


Figure 10: CMRI parameters, 4

Coming to the T1 CMRI finings, the average mid-segment (mean ± SD; 1062 ± 64 vs 1020 ± 8, $p < 0.001$) and apical segment (mean ± SD; 1065 ± 86 vs 1020 ± 4 , $p = 0.007$) T1 values were significantly higher in case group compared to control as was the total average T1 value in all segments (mean ± SD; 1057 ± 70 vs 1020 ± 4 , $p = 0.006$) . However there were no significant difference in basal segments (mean ± SD; 1044 ± 71 vs 1020 ± 5 , $p = 0.067$)**(Table 19, Figure 11).**

	Cases (mS) (N = 30)	Controls (mS) (N = 30)	p
BAS	1050 ± 59	1021 ± 16	0.013
BA	1047 ± 93	1020 ± 16	0.130
BAL	1051 ± 94	1020 ± 15	0.086
BIS	1021 ± 63	1023 ± 16	0.896
BI	1045 ± 68	1017 ± 16	0.030
BIL	1050 ± 125	1016 ± 16	0.147
B average	1044 ± 71	1020 ± 5	0.067
MAS	1080 ± 82	1019 ± 16	<0.001
MA	1056 ± 90	1021 ± 16	0.041
MAL	1041 ± 102	1020 ± 16	0.268
MIS	1100 ± 60	1023 ± 16	<0.001
MI	1056 ± 75	1017 ± 16	0.007
MIL	1037 ± 88	1022 ± 17	0.358
M average	1062 ± 64	1020 ± 8	<0.001
AAS	1069 ± 111	1019 ± 16	0.019
AA	1052 ± 131	1020 ± 16	0.184
AAL	1064 ± 100	1020 ± 16	0.023
AIS	1089 ± 112	1023 ± 17	0.002
AI	1072 ± 108	1020 ±16	0.013
AIL	1044 ± 85	1022 ± 15	0.152
A average	1065 ± 86	1021 ± 6	0.007
Total average	1057 ± 70	1020 ± 4	0.006

Table 19: T1 CMRI findings

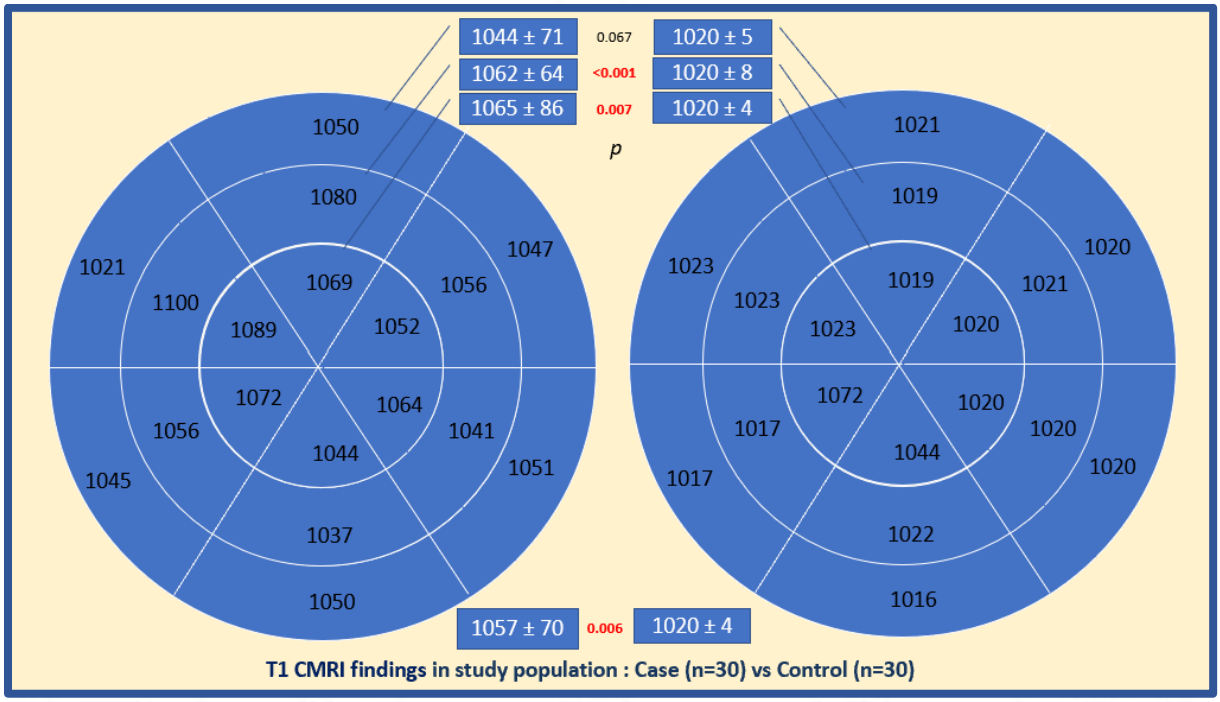
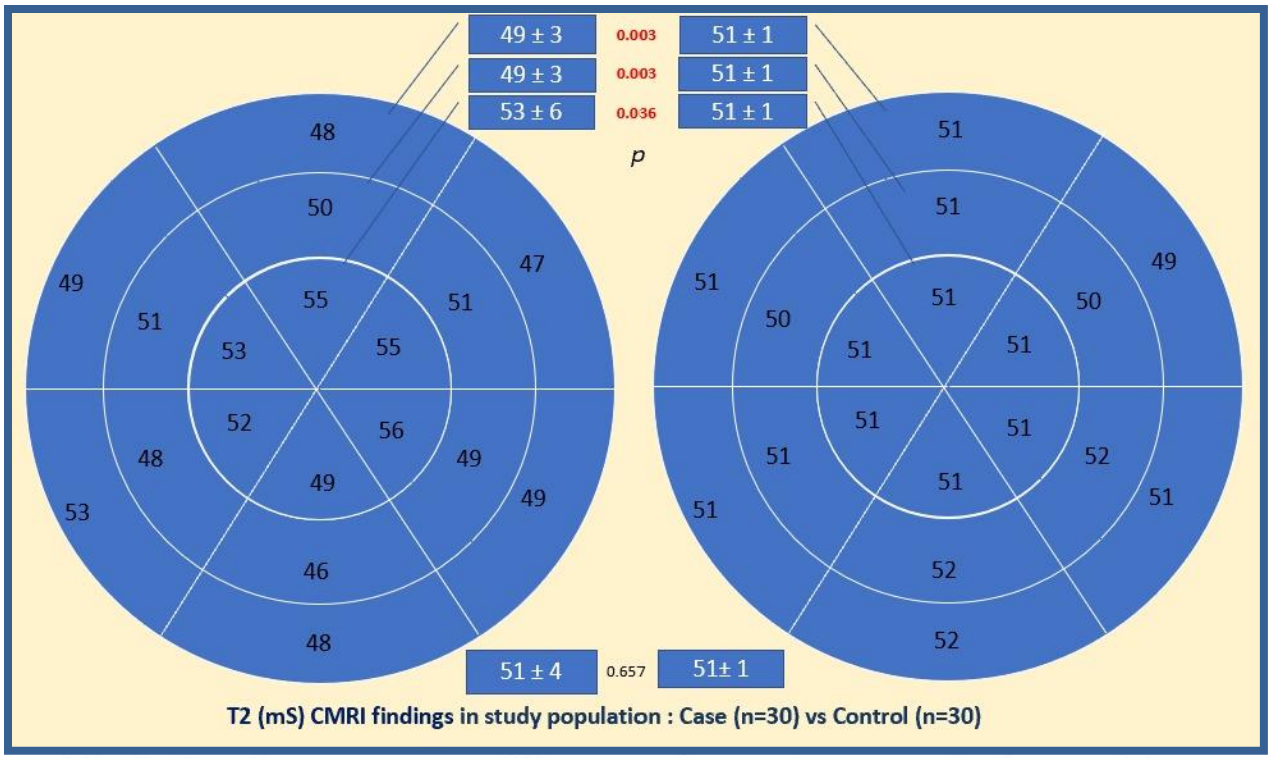


Figure 11: T1 CMRI findings

T2 CMRI analysis revealed that the average basal (mean ± SD; 49 ± 3 vs 47 ± 2, *p = 0.003*) , mid (mean ± SD; 49 ± 3 vs 47 ± 2, *p = 0.003*) and apical segment (mean ± SD; 53 ± 6 vs 49 ± 2, *p = 0.036*) T2 values were significantly higher in case group compared to control. However there were no significant difference in average T2 values (mean ± SD; 51 ± 4 vs 51 ± 1, *p = 0.*66)**.**



T2 (mS) CMRI findings in study population : Case (n=30) vs Control (n=30)

Figure 12: T2 CMRI findings

	Cases (mS) (N = 30)	Controls (mS) (N = 30)	p
BAS	48 ±7	51 ± 2	0.119
BA	47 ± 5	49 ± 1	0.018
BAL	49 ± 4	51 ± 2	0.022
BIS	49 ± 4	51 ± 2	0.045
BI	53 ± 5	51 ± 2	0.088
BIL	48 ± 4	52 ± 2	<0.001
B average	49 ± 3	51 ± 1	0.003
MAS	50 ± 5	51 ± 2	0.417
MA	51 ± 4	50 ± 2	0.565
MAL	49 ± 5	52 ± 2	0.004
MIS	51 ±3	50 ± 2	0.383
MI	48 ± 6	51 ± 2	0.014
MIL	46 ± 7	52 ± 2	<0.001
M average	49 ± 3	51 ± 1	0.003
AAS	55 ± 6	51 ± 2	<0.004
AA	55 ± 6	51 ± 2	<0.001
AAL	56 ± 6	51 ± 2	<0.001
AIS	53 ± 6	51 ± 2	0.171
AI	52 ± 9	51 ± 2	0.496
AIL	49 ±11	51 ± 2	0.428
A average	53 ± 6	51 ± 0.82	0.036
Total average	51 ± 4	51 ± 1	0.657

Table 20: T2 CMRI findings

Over a period of mean 25months [IQR 11-44months] follow up, we analyzed the data as following:

Among the 30 patients with HFpEF, we further analyzed our results into those who had a cardiac event during the period of follow up (Event group, n = 14)) and those who had an uneventful follow up during the course of this study (No event group, n = 16).

Out of 30 patients in case group, 14 patients (47%) had events in the form of index heart failure, out of which 4 patients (14% of total cases) had recurrent event (7% recurrent hospitalization for heart failure, 7% death) within a median follow up of 44 months and another 2 (7%) had follow up event of Ischemic stroke. Cumulative events including recurrent events were 67% **(Figure 13).**

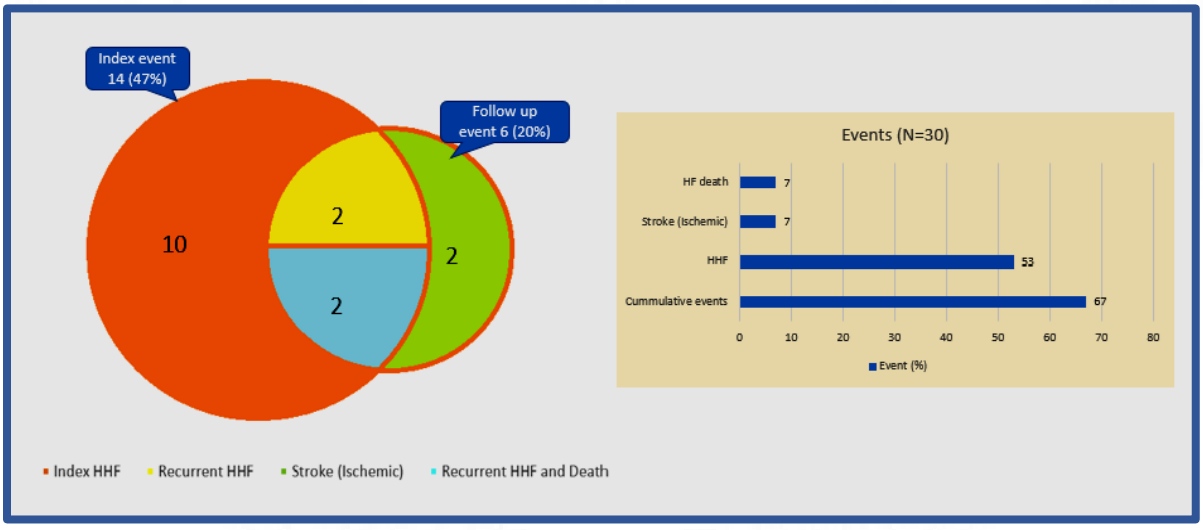


Figure 13: Cumulative events among cases of HFpEF

The mean age of the event group was 66 years which was higher compared to no-event group (60 years, p = 0.026). Both the group had female predominance with 88% female in the event group (p =1.00). There was no difference in height or body surface area in both the groups. According to the south-Asian consensus guidelines, 100% of the population in event group and 86% of the no-event group were obese with significant statistical difference between the groups (p <0.025) **(Figure 14, 15, Table 21).** The prevalence of hypertension, diabetes, hypothyroidism, chronic obstructive pulmonary disease, history of coronary artery disease, history of obstructive sleep apnea or prior COVID-19 infection were similar in both the groups **(Table 22)**.

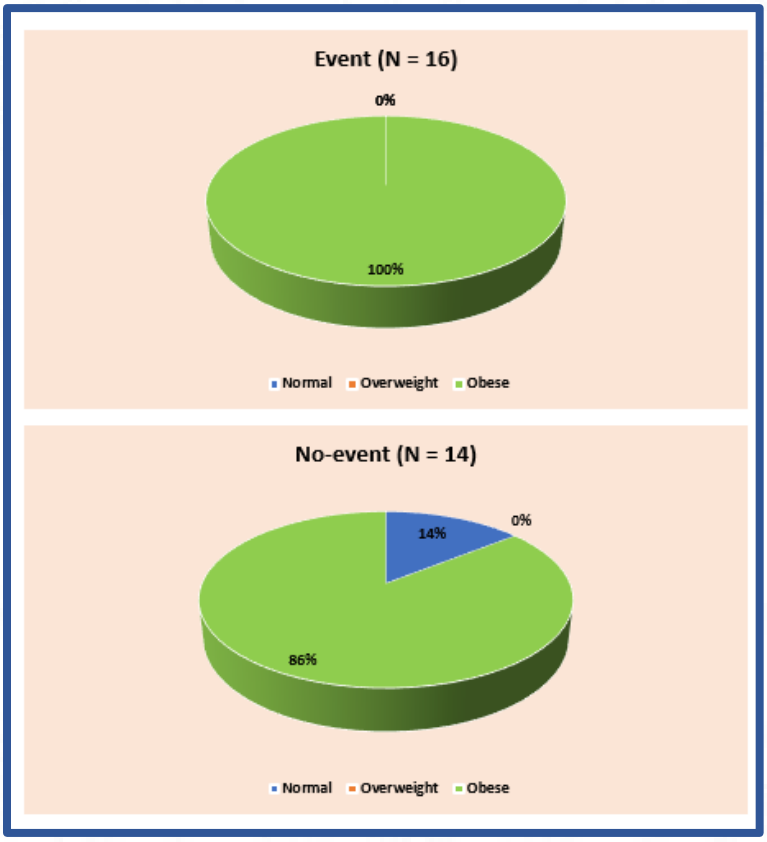


Figure 14: Incidence of obesity in event and no event groups

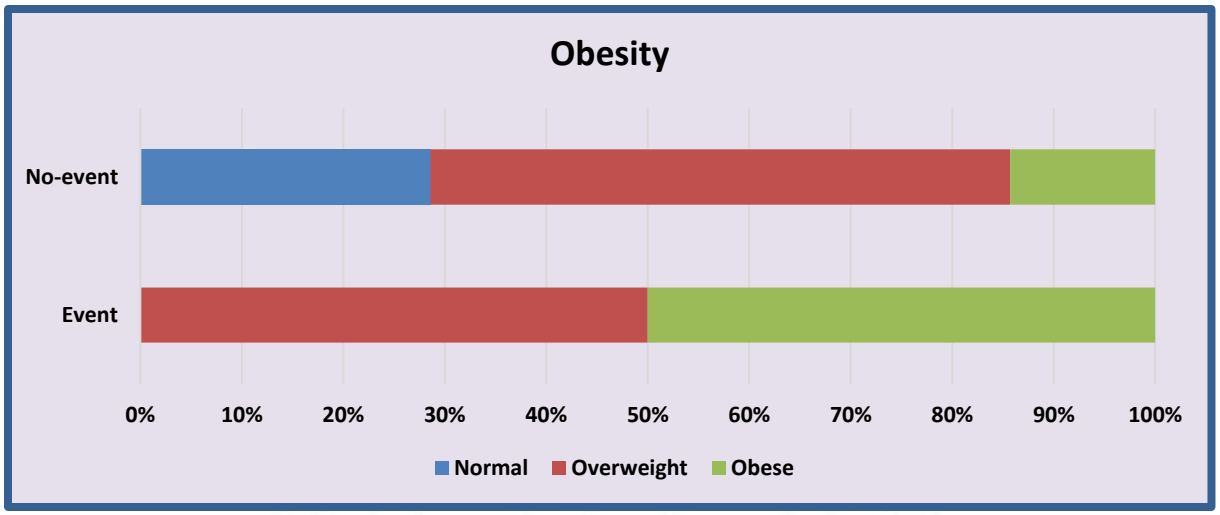


Figure 15: Distribution of body weight in event and no event groups

	Events (N = 16)	No events (N = 14)	p
Age (mean ±SD)	66 ± 6	60 ± 8	0.026
Female	14 (88%)	12 (86%)	1.000
Height (cm) (mean ±SD)	149 ± 7	152 ± 7	0.238
BMI (kg/m2) (mean ±SD)	29.6 ± 4.3	29.3 ± 5.43	0.859
BSA (m2) (mean ±SD)	1.60 ± 0.17	1.64 ± 0.19	0.511

Table 21: Demographic profile of HFpEF: Events versus no events

	Events (%) (N = 16)	No events (%) (N = 14)	p
DM	14 (88)	12 (86)	1.000
HTN	6 (38)	6 (43)	1.000
Hypothyroid	0	2 (14)	0.209
COPD	4 (25)	4 (29)	1.000
CAD	4 (25)	2 (14)	0.657
Dyslipidemia	8 (50)	8 (57)	0.730
Obesity	16 (100)	10 (71)	0.024
OSA	4 (25)	0	0.103
F/h CAD	0	2 (14)	0.209
H/O COVID	2 (13)	2 (14)	1.000
South-Asian Guidelines			
No obesity	0	4 (29)	0.025
Overweight	8 (50)	8 (57)	
Obese	8 (50)	2 (14)	
WHO guidelines			
No obesity	0	2 (14)	
Obese	16 (100)	14 (86)	

Table 22: Co-morbidities and personal history in HFpEF: Events versus no events

Focusing on the clinical features, patients in event group were more likely to have paroxysmal nocturnal dyspnoea (47% vs 0%, *p = 0.019*). However, there were no differences in terms of shortness of breath, cough, anasarca, urine output or history of palpitations **(Table 23)**.

	Events (%) (N = 16)	No events (%) (N = 14)	p
SOB	16	14	N/A
PND	6 (47)	0	0.019
Cough	8 (50)	2 (14)	0.058
Expectoration	0	0	N/A
Anasarca	1 (6)	0	1.000
Oliguria	0	0	N/A
Angina	0	6 (43)	0.005
Palpitation	8 (50)	4 (29)	0.284
Syncope	0	0	N/A

Table 23: Clinical presentation in HFpEF: Events versus no events

Patients in the event group had higher baseline heart rate (mean ± SD, 87 ± 25 bpm vs 72 ± 9 bpm; $p = 0.043$), respiratory rate (mean ± SD, 20 ± 7 per min vs 13 ±1 per min; $p < 0.001$), lower saturation in room air (mean ± SD, 95 ± 5 % vs 99 ± 1 %; $p = 0.019$), higher prevalence of elevated jugular venous pressure (38% vs 14%, $p = 0.019$) and gallop rhythm (38% vs 0%, $p = 0.019$). Both groups had uncontrolled hypertension at presentation with no differences between the groups **(Table 24)**.

	Events (N = 16)	No events (N = 14)	p
Pulse rate (bpm)	87 ± 25	72 ± 9	0.043
Low volume pulse, (%)	3 (19)	0	0.228
SBP (mmHg)	148 ± 38	159 ± 32	0.384
DBP (mmHg)	80 ± 14	85 ±10	0.239
Respiratory rate (/min)	20 ± 7	13 ±1	<0.001
Saturation @ RA (%)	95 ± 5	99 ±1	0.019
JVP, (%)	6 (38)	0	0.019
Rales, (%)	6 (38)	2 (14)	0.226
S1, (%)	16	14	
Loud P2, (%)	8 (50)	2 (14)	0.058
Gallop , (%)	6 (38)	0	0.019
Murmur, (%)	4 (25)	2 (14)	0.657
Pedal edema, (%)	8 (50)	2 (14)	0.058

Table 24: Clinical findings in HFpEF: Events versus no events

The NT-Pro-BNP at presentation was significantly higher in event group compared to no-event group (mean ± SD, 5550 ± 9160 pg/mL vs 455 ± 375 pg/mL; *p = 0.047*). There were no differences in terms of hemoglobin and renal function parameters in both the groups.

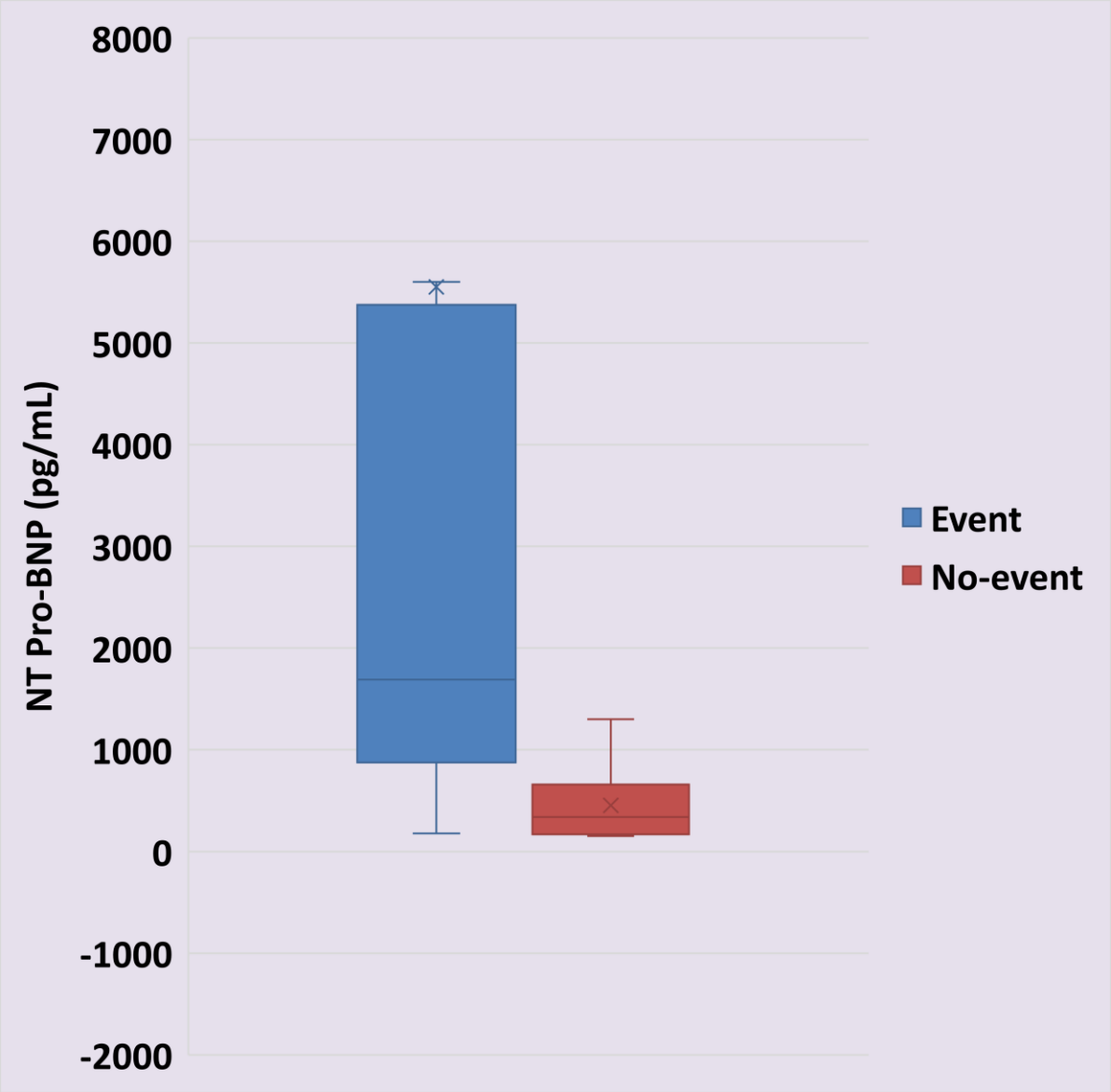


Figure 16: NT-Pro-BNP among event and no-event groups in HFpEF

	Events (N = 16)	No events (N = 14)	p
Hb g/dL (mean ±SD)	13.1 ± 1.9	13.1 ± 1.2	0.974
Creatinine mg/dL (mean ±SD)	1.00 ± 0.34	1.01 ± 0.15	0.876
TSH mIU /L (mean ±SD)	2.49 ± 0.69	3.39 ± 1.05	0.009
Pro-BNP pg/mL (mean ±SD)	5550 ± 9160	455 ± 375	0.047

Table 25: Lab reports in HFpEF: Event versus no event

Only 38% in event group and 14% in no-event group were on SGLT2 inhibitor therapy with no difference among groups. 14 (88%) patients in event group and 10 (71%) in no-event group were on loop diuretics. Average frusemide equivalent dose in event group was 43mg (SD 21mg) and 20mg (SD 12mg) in no-event group with significant difference (*p = 0.005*). Mineralocorticoid receptor antagonist (MRA) use was not different in both the groups (50% vs 57%). However MRA dose was higher in event group (31 ± 4 vs 19 ± 2 mg/day, *p = 0.019*)

	Events (N = 16)	No events (N = 14)	p
SGLT2i (%)	6 (38)	2 (14)	0.226
Loop Diuretics (%)	14 (88)	10 (71)	0.378
Frusemide equivalent, mg/d	43 ± 21 (n=14)	20 ± 12 (n=10)	0.005
MRA (%)	8 (50)	8 (57)	0.730
MRA dose, mg / day	31 ± 4 (n=8)	19 ± 2 (n=8)	0.019

Table 26: Medication use in HFpEF: Events versus no events

There was no difference between event and no-event group in terms of rhythm, left atrial enlargement in electrocardiogram, QRS axis, QRS duration, ST-T changes. PR interval was relatively longer but within normal limit in event group (169 ± 25 vs 146 ± 14 mS , *p = 0.011*).

	Events (N = 16)	No events (N = 14)	p
Sinus rhythm , %	12 (75)	12 (86)	0.657
LAE (n=24), %	4 (33)	4 (33)	1.000
PR duration (n=24), mS	169 ± 25	146 ± 14	0.011
QRS Axis, degree	26 ± 47	28 ± 26	0.883
QRS duration , mS	91 ± 32	85 ± 30	0.619
QTC, mS	396 ± 25	414 ±13	0.025
LVH, %	2 (13)	2 (14)	1.0
ST T changes , %	8 (50%)	8 (57%)	0.730

Table 27: ECG findings in HFpEF: Events versus no events

Cardiac enlargement was present in 88% (vs 57%, p= 0.101) of the event group with mean cardio-thoracic ratio being 61% compared to 52% in no-event group, which was statistically significant (p <0.001). Left atrial enlargement (Carinal angle >75 degree) was found in 88% of the event group compared to 29% in no-event group (p = 0.002). All patients in event group had chest x-ray evidence of pulmonary venous hypertension with grade 1, 2 and 3 being equitably distributed. In contrast, most of the patients (86%) in no-event group had grade 1 pulmonary venous hypertension, with none having grade 2 or 3 (p of interaction 0.025) **(Table 28, Figure 17, 18).**

	Events (%) (N = 16)	No events (%) (N = 14)	p
CE	14 (88)	8 (57)	0.101
CTR, %	61 ± 6	52 ± 4	<0.001
LAE	14 (88)	4 (29)	0.002
Carinal angle, degree	84 ± 9	77 ± 8	0.031
PVH Grade			
0	0	2 (14)	0.025
1	6 (38)	12 (86)	
2	5 (31)	0	
3	5 (31)	0	
PAH	16 (100)	4 (29)	<0.001
Lung field abnormalities	4 (25)	0	0.103

Table 28: CXR findings in HFpEF: Events versus no events

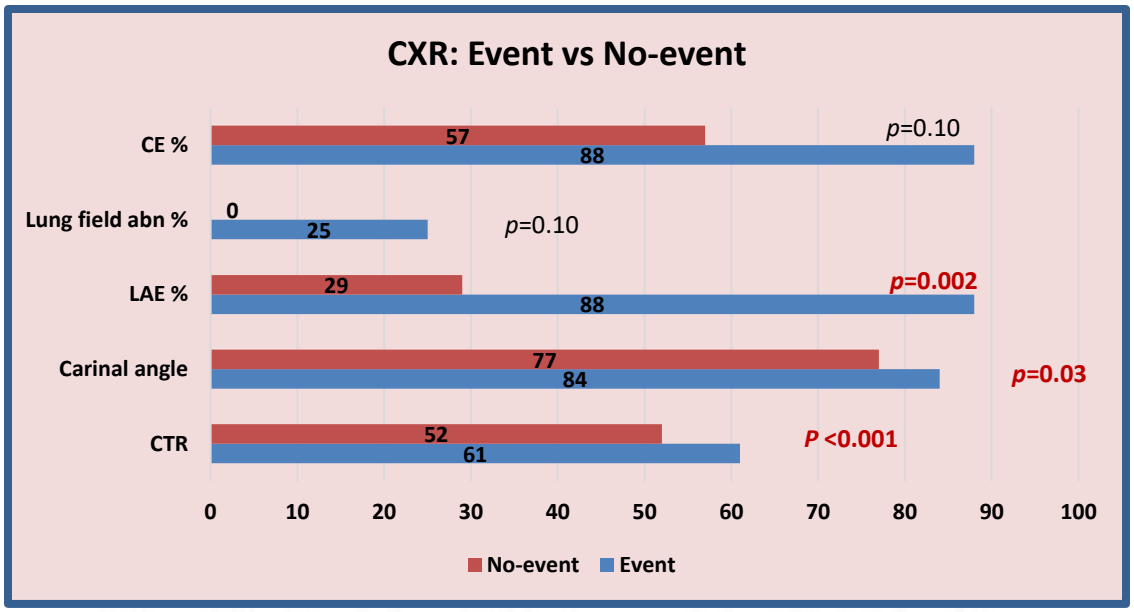


Figure 17: CXR findings in HFpEF: Events versus no events

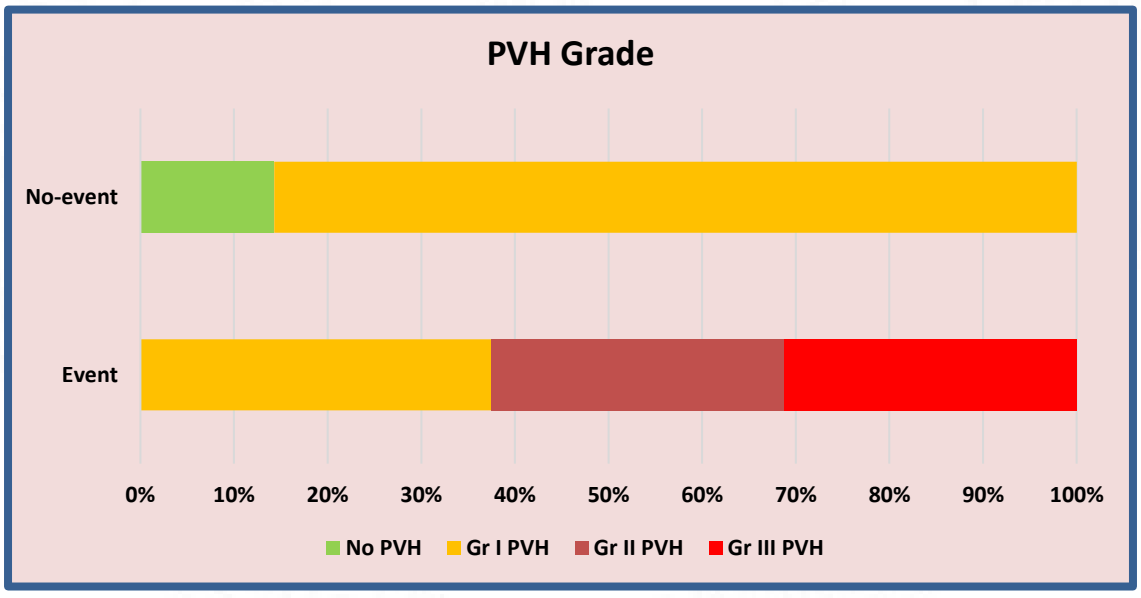


Figure 18: PVH in HFpEF: Events versus no events

There were no significant difference noted between event and no-event group in terms of echocardiographic evidence of left ventricular hypertrophy (p = 0.46), diastolic left ventricular internal dimension (p = 0.142), septal thickness (p = 0.101), left ventricular mass index (p = 0.311) or relative wall thickness (p = 0.127) **(Table 29).**

	Events (N = 16)	No events (N = 14)	p
LVIDD, mm	44.6 ± 3.8	46.6 ± 3.2	0.142
LVIDS, mm	28.0 ± 2.6	28.9 ± 3.7	0.466
IVS D, mm	12.6 ± 2.8	11.3 ± 1.1	0.101
IVS S, mm	14.8 ± 2.5	13.6 ± 1.3	0.122
PW D, mm	11.5 ± 2.4	10.6 ± 0.9	0.180
PW S, mm	13.8 ± 2.1	13.3 ± 1.9	0.527
LV mass (ASE), gm	198 ± 47	183 ± 18	0.268
LV mass index (ASE), gm/m^2	126 ± 36	113 ± 16	0.222
LV mass (Th), gm	177 ± 36	167 ± 14	0.311
LV mass index (Th), gm/m^2	112 ± 28	103 ± 13	0.321
RWT	0.53 ± 0.15	0.46 ± 0.06	0.127
Hypertrophy (%)			
Concentric Hypertrophy	8 (50)	8 (57)	0.460
Concentric Remodeling	2 (13)	0	
Eccentric Hypertrophy	2 (13)	4 (29)	
Normal	4 (25)	2 (14)	
LVH on Echo	10 (63)	11 (79)	0.440

Table 29: Echocardiography findings [1] in HFpEF: Events versus no events

There were no differences between event and no-event group in terms of ejection fraction, LA volume index, Average E/e', left ventricular diastolic dysfunction grade, mitral regurgitation or tricuspid regurgitation gradient. However, statistical difference was evident in 63% of the patients in event group having mild pericardial effusion compared to none in no-event group (*p <0.001*) **(Tables 30, 31, 32).**

	Events (N = 16)	No events (N = 14)	p
RVID, mm	23.6 ± 2.6	23.4 ± 4.3	0.880
EF, %	66 ± 8	65 ± 6	0.547
FC, %	37 ± 6	38 ± 6	0.596
LA PLAX, mm	41.2 ± 5.0	41.4 ± 4.6	0.924
LA A4C L, mm	57.5 ± 5.8	53.9 ± 7.6	0.148
LA A4C W, mm	41.4 ± 5.8	41 ± 5.9	0.841
LAV, mL	51.6 ± 12.5	49.6 ± 20.1	0.737
LAV I , mL/m2	32.8 ± 9.5	30.0 ± 9.8	0.433
Aorta, mm	29.1 ± 4.9	29.7 ± 1.9	0.678
RWMA, %	2 (13)	0	0.485

Table 30: Echocardiography findings [2] in HFpEF: Events versus no events

	Events (N = 16)	No events (N = 14)	p
MV E, m/s	1.01 ± 0.42	1.14 ± 0.13	0.280
MV A, m/s	0.90 ± 0.27	0.89 ± 0.22	0.855
EDT (mS)	157 ± 41	150 ± 15	0.568
L wave (%)	2 (13)	4 (29)	0.378
LAT E', cm/s	7.2 ± 2.2	8.0 ± 2.3	0.310
LAT E/E'	14.7 ± 5.0	16.7 ± 9.2	0.459
MED E', cm/s	5.9 ± 1.2	5.7 ± 1.4	0.572
MED E/E'	17.0 ± 5.5	22.1 ± 8.7	0.066
AVG E/E'	15.9 ± 5.0	19.4 ± 8.9	0.185
LAT A', cm/s	9.8 ± 3.8	7.9 ± 1.7	0.119
MED A', cm/s	8.7 ± 3.2	8.3 ± 2.7	0.719

Table 31: Echocardiography findings [3] in HFpEF: Events versus no events

	Events (N = 16), %	No events (N = 14), %	p
TR Grade			
0	2 (12)	0	0.007
1	0	4 (29)	
2	14 (88)	8 (57)	
3	0	2 (14)	
TR Gradient, mmHg	34 ± 1	35 ± 3	0.811
LVDD Grade 1	6 (38)	4 (29)	0.881
LVDD Grade 2	8 (50)	8 (57)	
LVDD Grade 3	2 (12)	2 (14)	
TAPSE	20.6 ± 2.5	19.9 ± 0.4	0.314
AOV , m/s	1.43 ± 0.29	1.21 ± 0.1	0.048
PV, m/s	1.01 ± 0.17	1.04 ± 0.0	0.621
MR			
0	0	2 (14)	0.591
1+	4 (25)	2 (14)	
2+	10 (63)	8 (57)	
3+	2 (12)	2 (14)	
AR	2 (13)	2 (14)	1.000
AS	2 (13)	0	0.485
PE	10 (63)	0	0.000
GLS	10 (71)	10 (63)	0.709

Table 32: Echocardiography findings [4] in HFpEF: Events versus no events

20 patients (66%) had left ventricular global longitudinal strain abnormality (GLS) in at least one of 18 segments. However there was no significant difference in peak strain value among event and no-event group except in apical antero-lateral segment **(Figure 19, Table 33)**.

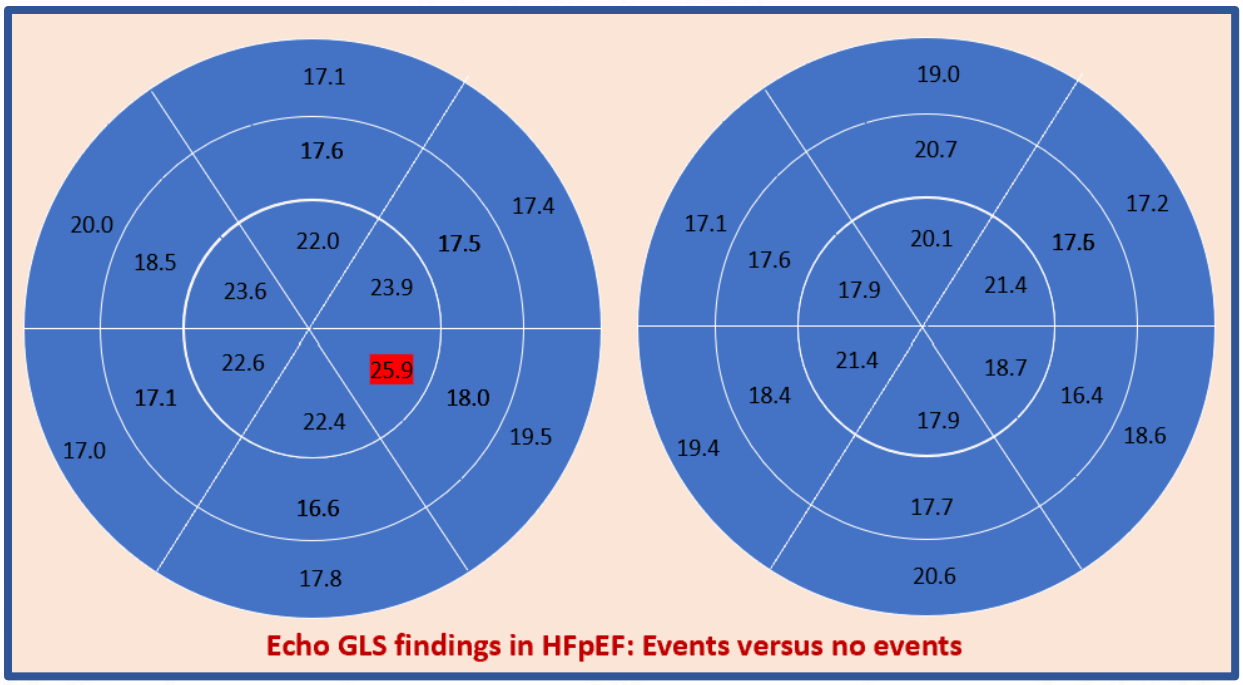


Figure 19: Echo GLS findings in HFpEF: Event versus no event

	Events (-%) (N = 16)	No events (-%) (N = 14)	p
BAS	17.1 ± 5.7	19.0 ± 1.2	0.329
BA	17.4 ± 8.4	17.2 ± 1.7	0.933
BAL	19.5 ± 7.3	18.6 ± 1.8	0.724
BIS	20.0 ± 3.4	17.1 ± 1.5	0.100
BI	17.0 ± 6.2	19.4 ± 1.2	0.230
BIL	17.8 ± 7.4	20.6 ± 1.0	0.103
MAS	17.6 ± 6.5	20.7 ± 1.6	0.191
MA	17.5 ± 7.0	17.6 ± 2.0	0.722
MAL	18.0 ± 7.4	16.4 ± 2.1	0.575
MIS	18.5 ± 6.4	17.6 ± 2.1	0.722
MI	17.1 ± 4.9	18.4 ± 1.6	0.520
MIL	16.6 ± 8.7	17.7 ± 1.5	0.690
AAS	22.0 ± 7.6	20.1 ± 1.8	0.680
AA	23.9 ± 5.8	21.4 ± 1.8	0.290
AAL	25.9 ± 9.5	18.7 ± 2.0	0.031
AIS	23.6 ± 10.3	17.9 ± 2.4	0.116
AI	22.6 ± 9.4	21.4 ± 1.7	0.689
AIL	22.4 ± 4.9	17.9 ± 1.6	0.187

Table 33: Echo GLS findings in HFpEF: Events versus no events

Coming to the cath lab findings, 4 patients (25%) in event group and 2 patients (14%) in no-event group had minor coronary artery disease (*p = 0.657*). 8 patients (50%) in event group and 2 patients (14%) in no-event group underwent cardiac catheterization study with no difference in pulmonary artery mean pressure (24.5 ± 1.1 vs 26 ± 0.0 mmHg , *p = 0.539*), pulmonary capillary wedge pressure (17.8 ± 1.7 vs 12 ± 0.0 mmHg , *p = 0.153*), left ventricular end-diastolic pressure (17 ± 5.8 vs 10 ± 0.0 mmHg , *p = 0.142*) or pulmonary vascular resistance (2.5 ± 0.9 vs 3.3 ± 0.0 WU , *p = 0.256*) **(Table 34)**.

	Events (N = 16)	No events (N = 14)	p
CAD in CAG (%)	4 (25)	2 (14)	0.657
Predominant vessel involved	LAD 2, LCX 2	RCA 2	0.177
PA mean, mmHg	24.5 ± 1.1	26 ± 0	0.539
PCWP, mmHg	17.8 ± 1.7 (n=8)	12 ± 0 (n=2)	0.153
LVED, mmHg	17 ± 5.8 (n=8)	10 (n=2)	0.142
PVR, WU	2.5 ± 0.9 (n=8)	3.3 (n=2)	0.256

Table 34: Cath findings in HFpEF: Events versus no events

MRI derived left ventricular internal diameter were similar in both event and no-event group. However diastolic interventricular septal thickness (mean ± SD, 10.9 ± 2.7 vs 8.6 ± 2.0 mm , $p = 0.016$) and posterior wall thickness (mean ± SD, 10.1 ± 2.5 vs 7.1 ± 1.1 mm , $p < 0.001$) were significantly higher in event group. Right ventricular internal diameter and LA volume index were similar in both the groups **(Table 35, Figure 20).**

	Events (N = 16)	No events (N = 14)	p
LVIDD, mm	45.8 ± 3.9	47.7 ± 4.1	0.199
LVIDS, mm	29.8 ± 5.3	29.1 ± 6.8	0.764
IVS D, mm	10.9 ± 2.7	8.6 ± 2.0	0.016
IVS S, mm	15.6 ± 2.3	13.8 ± 2.1	0.028
PW D, mm	10.1 ± 2.5	7.1 ± 1.1	<0.001
PW S, mm	16.5 ± 2.2	12.4 ± 2.6	<0.001
RVID, mm	43.2 ± 3.0	43.1 ± 5.2	0.940
LV mass, gm	94 ± 29	88 ± 29	0.606
LV mass index, gm/m^2	59 ± 19	55 ± 21	0.584
LA 4C L, mm	48.6 ± 4.6	47.9 ± 5.6	0.712
LA 4C W, mm	48.4 ± 4.8	47.1 ± 6.1	0.497
LA, mm	45.4 ± 4.2	43.9 ± 6.4	0.427
LAV, mL	57 ± 13	52 ± 17	0.448
LAVI, mL/m2	36 ± 11	32 ± 7	0.186

Table 35: CMRI findings in HFpEF [1]: Events versus no events

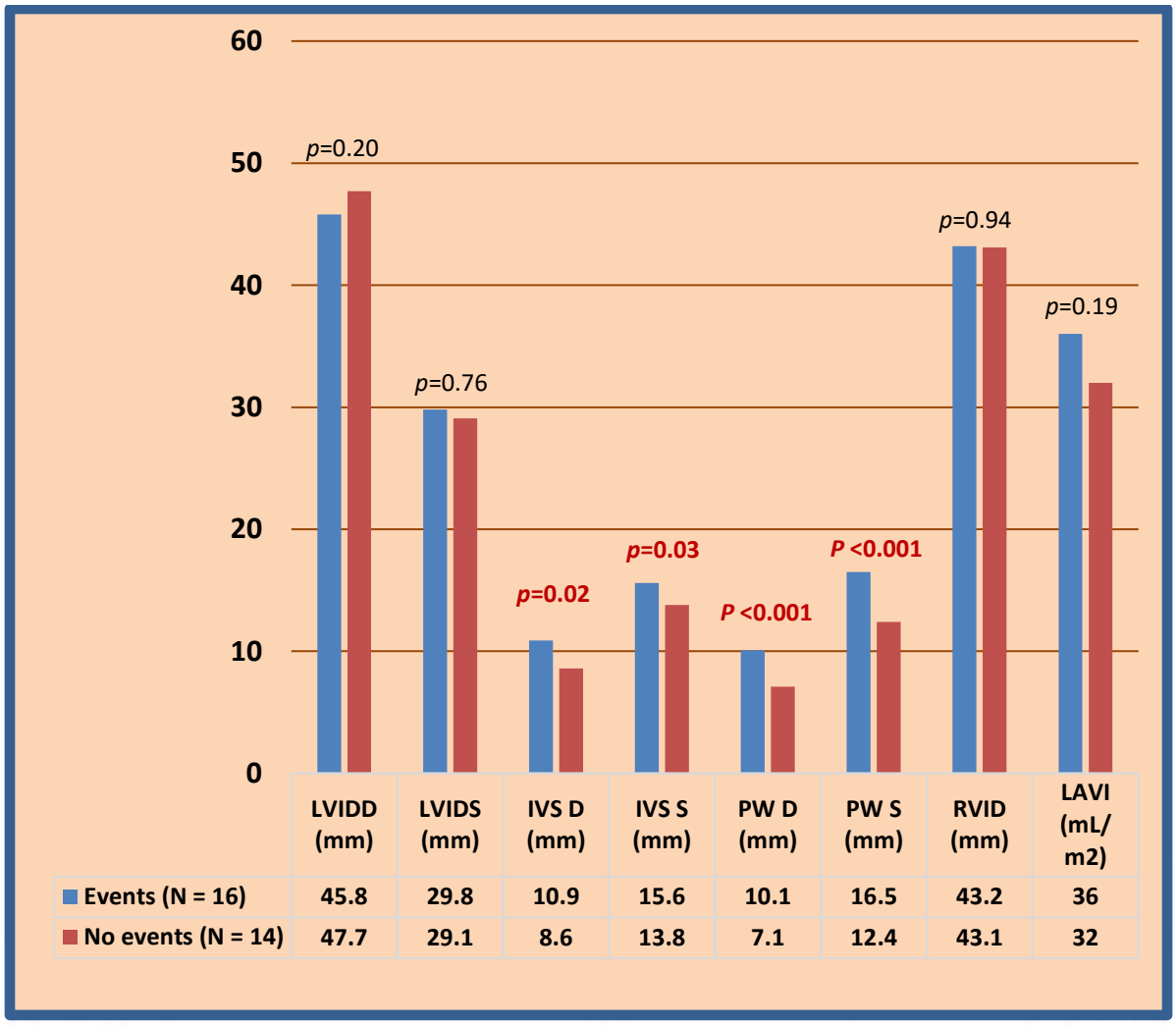


Figure 20: CMRI derived findings in HFpEF 1: Events versus No events

MRI derived left ventricular mass index were similar in both the group as were left ventricular end diastolic, systolic volumes and stroke volume index. Left ventricular ejection fraction was lower in event group compared to no-event group (mean ± SD, 63 ± 4 vs 68 ± 7 % , *p = 0.023*). Right ventricular stroke volume index (mean ± SD, 32 ± 8 vs 40 ± 7 mm , *p = 0.010*) and ejection fraction (mean ± SD, 53 ± 8 vs 60 ± 10 % , *p = 0.034*) were lower in event group compared to no-event group. There was no difference of left or right ventricular cardiac output by CMRI **(Table 36, Figure 21, 22, 23)**.

	Events (N = 16)	No events (N = 14)	P
LV ED Vol, mL	101 ± 22	112 ± 13	0.123
LV ED Vol index, mL/m2	64 ± 17	68 ± 5	0.396
LV ES Vol, mL	37 ± 9	36 ± 10	0.672
LV ES Vol index, mL/m2	24 ± 7	22 ± 5	0.393
LV SV, mL	64 ± 14	76 ± 12	0.016
LV SV index, mL/m2	41 ± 11	47 ± 6	0.065
LV CO, L/min	4.48 ± 1.18	4.98 ± 1.05	0.230
LV CO index, L/min/m	2.82 ± 0.82	3.05 ± 0.61	0.395
LV EF, %	63 ± 4	68 ± 7	0.023
RV ED Vol, mL	98 ± 23	111 ± 24	0.137
RV ED Vol index, mL/m2	61 ± 12	67 ± 8	0.131
RV ES Vol, mL	47 ± 13	46 ± 15	0.822
RV ES Vol index, mL/m2	29 ± 7	28 ± 8	0.608
RV SV, mL	52 ± 15	66 ± 16	0.012
RV SV index, mL/m2	32 ± 8	40 ± 7	0.010
RV CO, L/min	3.86 ± 1.24	4.54 ± 1.43	0.170
RV CO index, L/min/m^2	2.40 ± 0.73	2.74 ± 0.77	0.219
RV EF, %	53 ± 8	60 ± 10	0.034
LGE, %	4 (25)	4 (29)	1.000

Table 36: CMRI findings in HFpEF [2]: Events versus no events

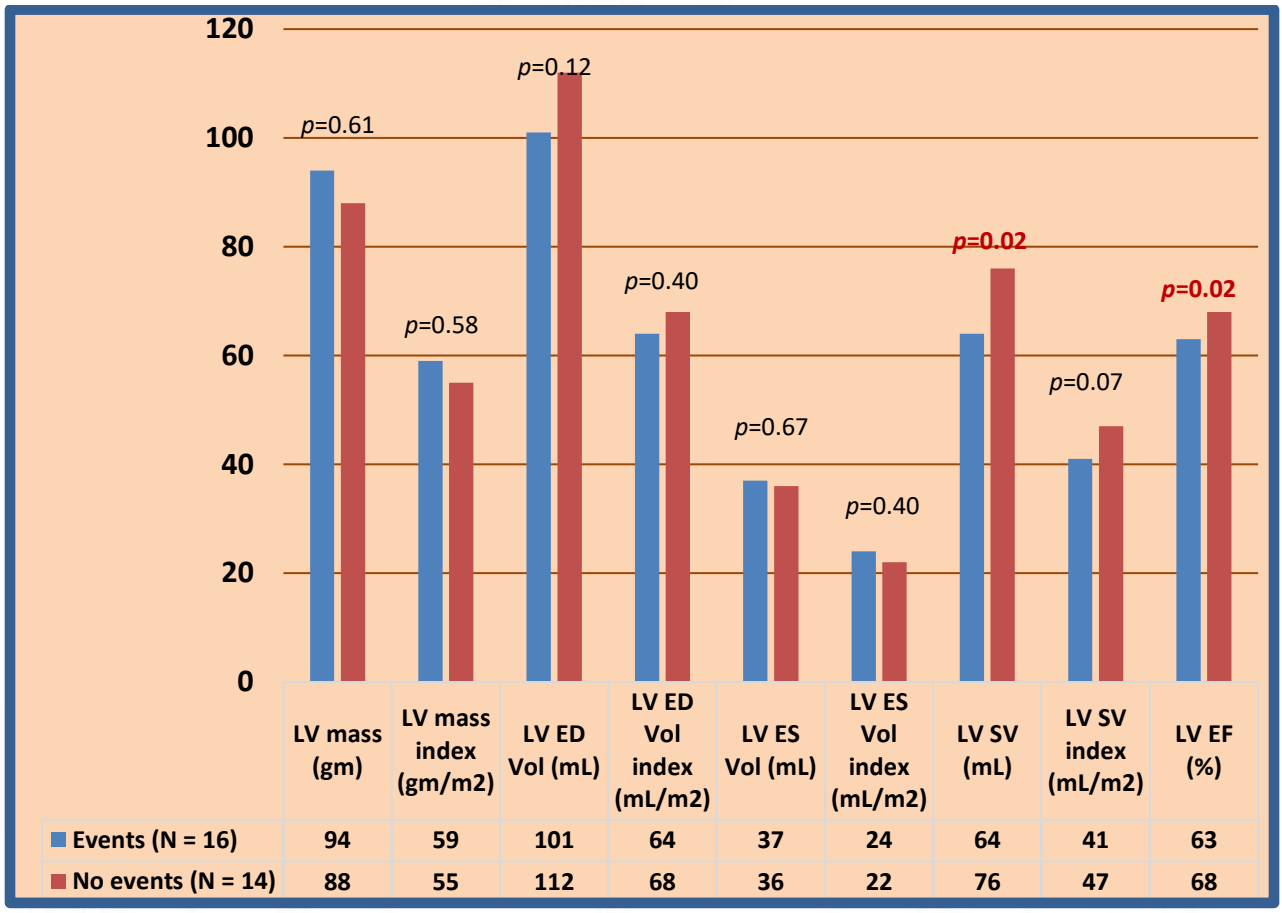


Figure 21: CMRI derived findings in HFpEF 2: Events versus No events

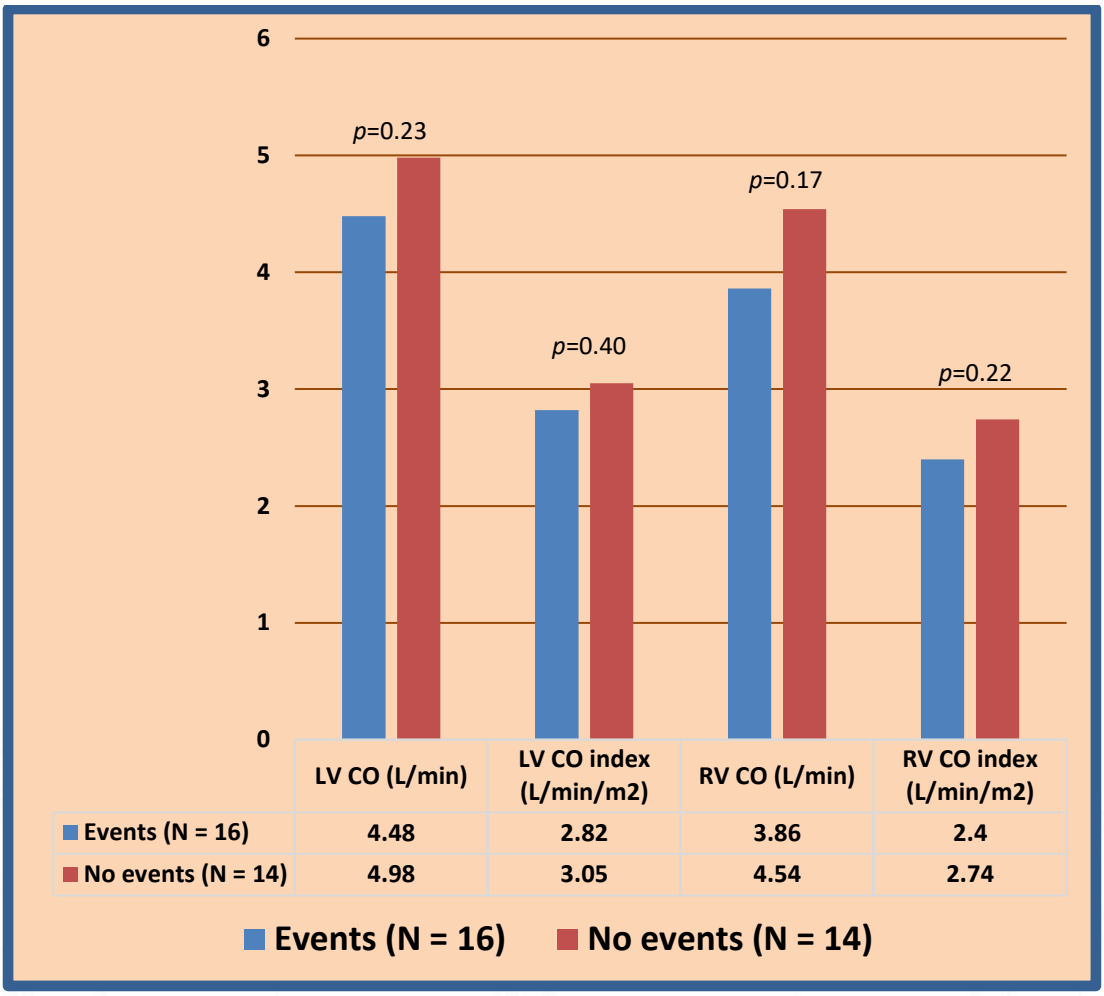


Figure 22: CMRI derived findings in HFpEF 3: Events versus No events

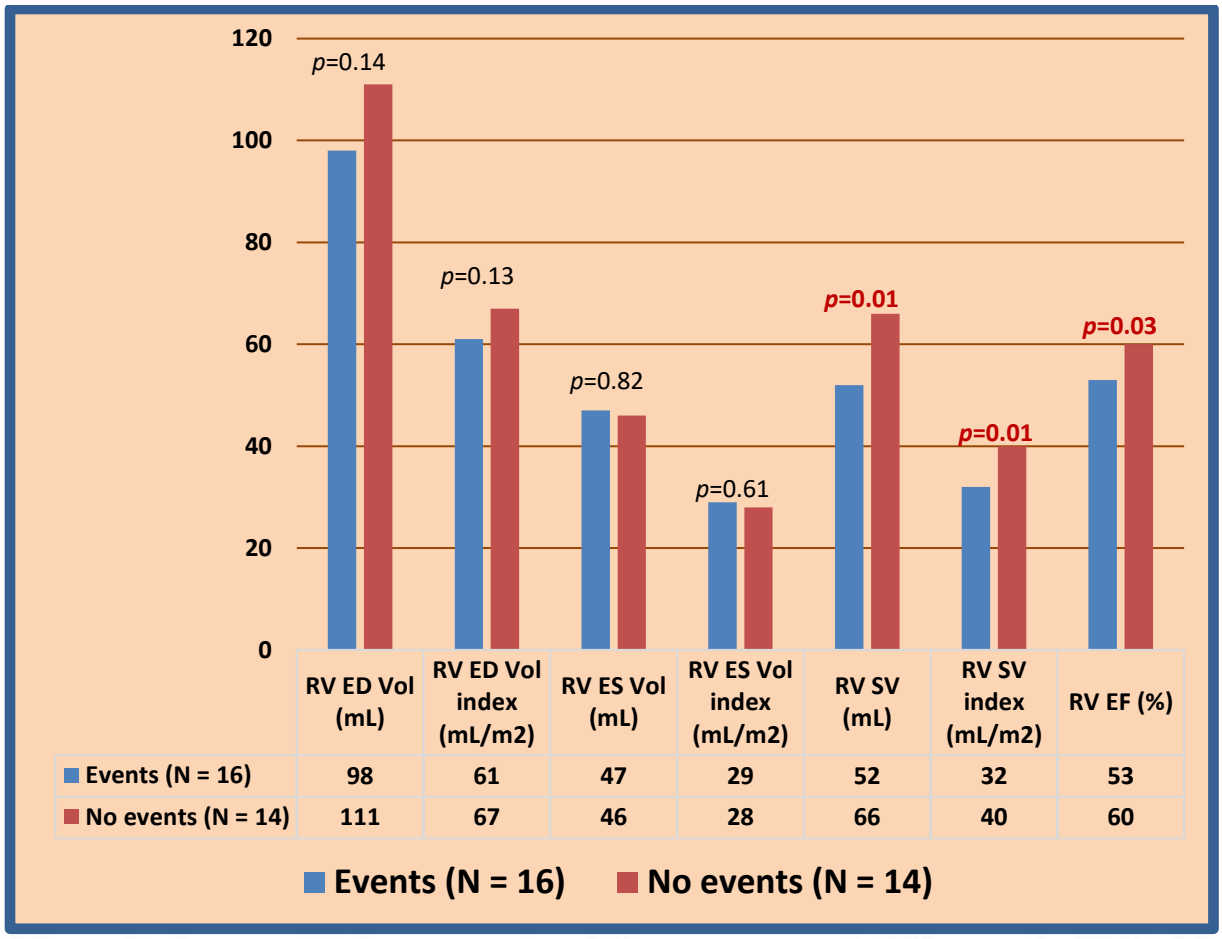


Figure 23: CMRI derived findings in HFpEF 4: Events versus No events

8 subjects (27%) in event group had late gadolinium enhancement (LGE) compared to none in control group (*p = 0.005*). There was no difference in LGE among event and no-event group. There was no sub-epicardial LGE, while sub-endocardial and mid-myocardial LGE were shared equally (50% each). LGE was seen only in basal segments and predominantly involving anteroseptal (75% of LGE group) and infero-septal (100% of LGE group)segments followed by inferior wall (25%) and infero-lateral wall (25%) **(Figure 24, 25, 26)**.

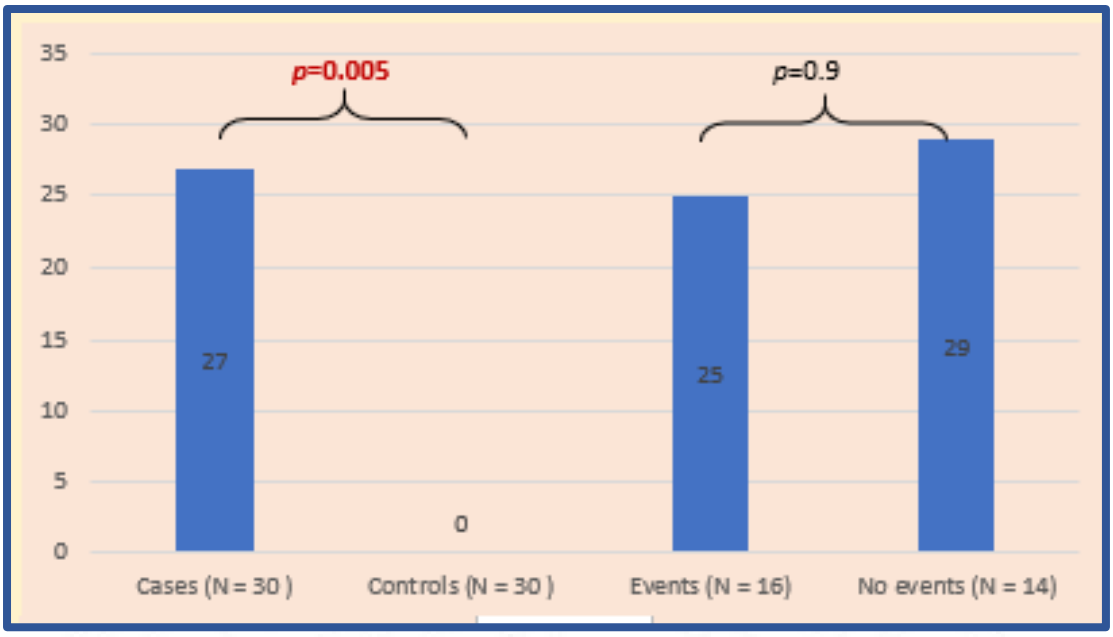


Figure 24: LGE on CMRI: Events versus no events (% in bar diagram)

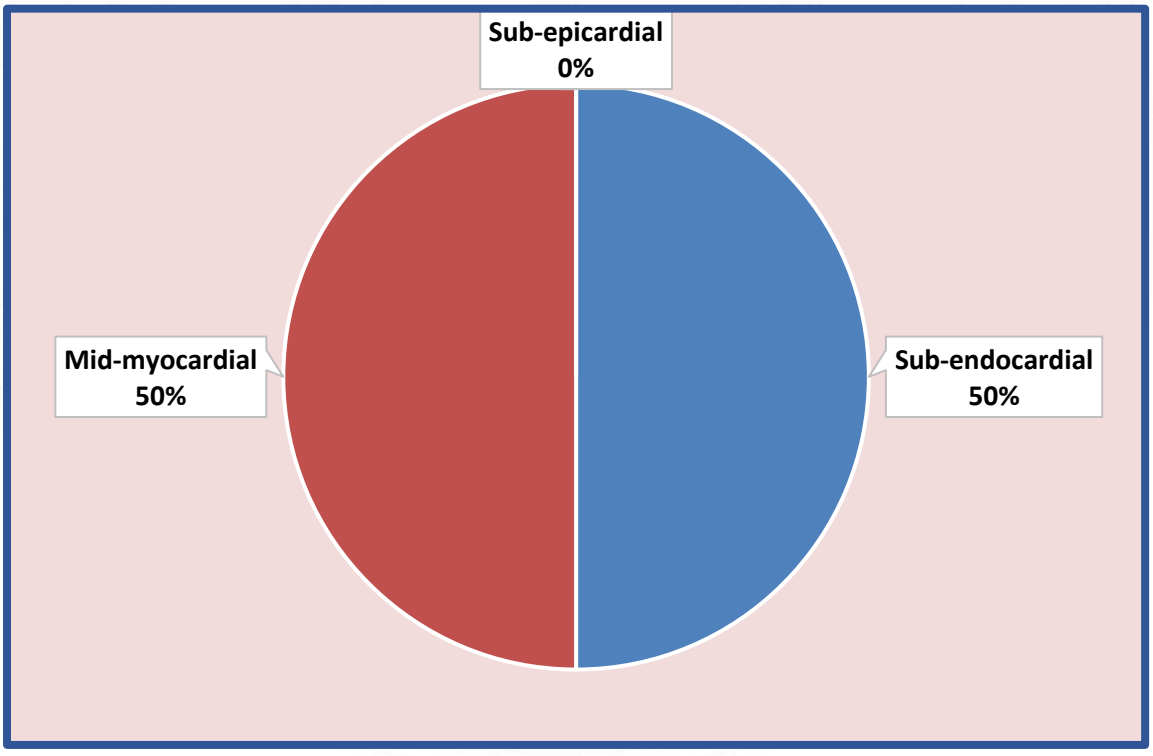


Figure 25: Distribution of LGE on CMRI 1

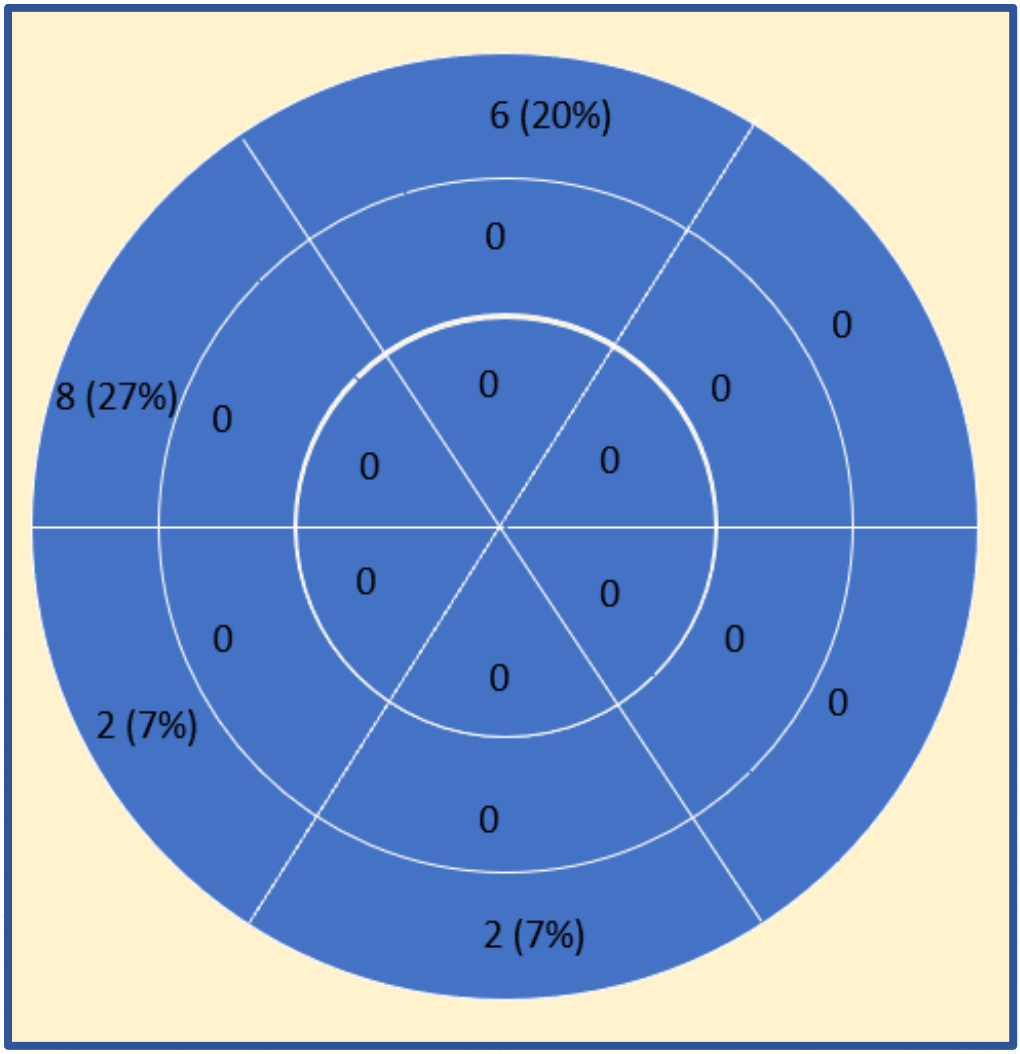


Figure 26: Distribution of LGE on CMRI 2

Average basal (mean ± SD; 1087 ± 72 vs 994 ± 18 , *p < 0.001)*, mid-segment (mean ± SD; 1099 ± 67 vs 1019 ± 17, *p < 0.001*) and apical segment (mean ± SD; 1116 ± 91 vs 1001 ± 18, *p < 0.001*) T1 values were significantly higher in event group compared to no-event as was the total average T1 value in all segments (mean ± SD; 1101 ± 70vs 1007 ± 15, *p < 0.001*) **(Table 37, Figure 27).**

	Events (mS) (N = 16)	No events (mS) (N = 14)	p
BAS	1085 ± 60	1010 ± 19	<0.001
BA	1108 ± 82	978 ± 35	<0.001
BAL	1108 ± 84	984 ± 53	<0.001
BIS	1037 ± 76	1003 ± 41	0.154
BI	1059 ± 92	1030 ± 10	0.259
BIL	1126 ± 125	963 ± 40	<0.001
B average	1087 ± 72	994 ± 18	<0.001
MAS	1119 ± 91	1035 ± 36	0.003
MA	1102 ± 99	1003 ± 32	0.001
MAL	1093 ± 105	982 ± 57	0.002
MIS	1120 ± 59	1077 ± 55	0.048
MI	1089 ± 59	1019 ± 75	0.008
MIL	1071 ± 100	998 ± 52	0.020
M average	1099 ± 67	1019 ± 17	<0.001
AAS	1110 ± 127	1022 ± 69	0.030
AA	1110 ± 143	986 ± 76	0.007
AAL	1108 ± 112	1014 ± 53	0.008
AIS	1122 ± 139	1051 ± 53	0.083
AI	1129 ± 109	1006 ± 61	<0.001
AIL	1116 ± 31	963 ± 40	<0.001
A average	1116 ± 91	1001 ± 18	<0.001
Total average	1101 ± 70	1007 ± 15	<0.001

Table 37: T1 CMRI findings in HFpEF: Events versus no events

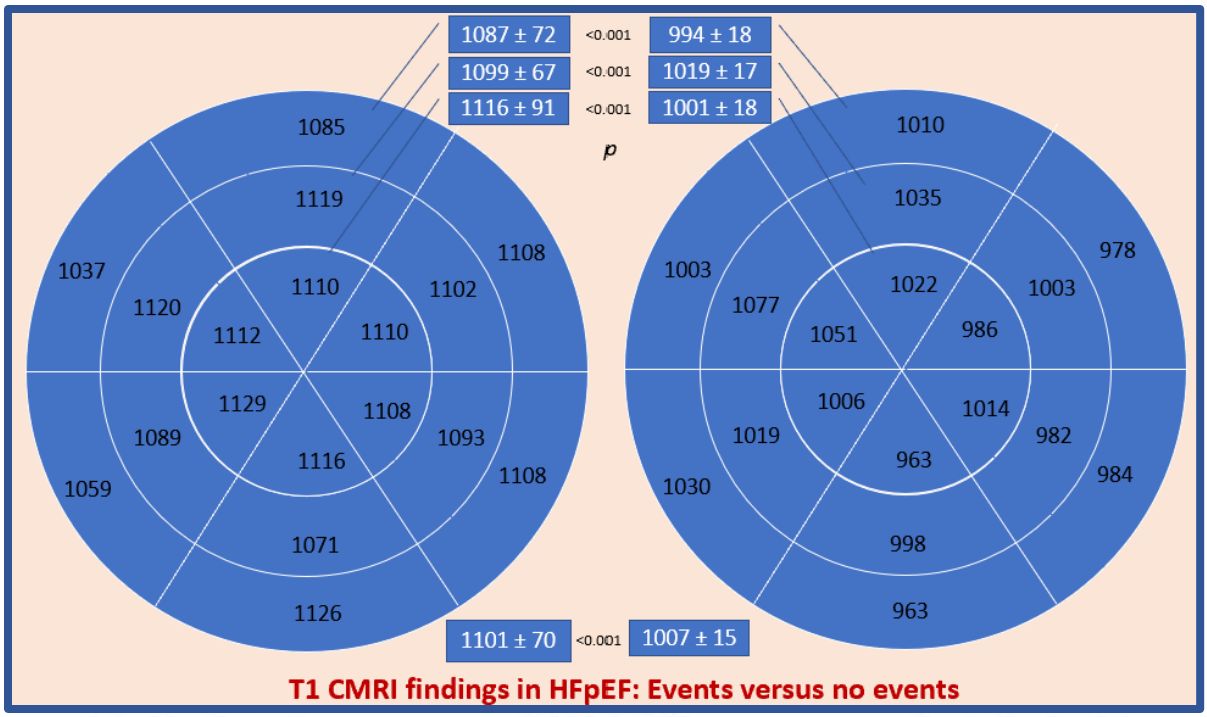


Figure 27: T1 CMRI findings in HFpEF: Events versus no events

The T2 CMRI findings revealed an average basal (mean ± SD; 51 ± 3 vs 47 ± 2 , $p = 0.001$) , mid (mean ± SD; 51 ± 3 vs 47 ± 2 , $p < 0.001$), apical segment (mean ± SD; 57 ± 6 vs 49 ± 2 , $p < 0.001$) and total (mean ± SD; 53 ± 3 vs 48 ± 2 , $p < 0.001$) T2 values, all of which were significantly higher in event group compared to no-event group **(Table 38, Figure 28)**.

	Events (mS) (N = 16)	No events (mS) (N = 14)	p
BAS	51 ± 9	46 ± 3	0.056
BA	49 ± 5	45 ± 4	0.082
BAL	51 ± 4	48 ± 5	0.027
BIS	50 ± 5	48 ± 3	0.160
BI	53 ± 7	52 ± 2	0.326
BIL	50 ± 4	46 ± 3	0.008
B average	51 ± 3	47 ± 2	0.001
MAS	54 ± 4	46 ± 2	<0.001
MA	52 ± 4	49 ± 3	0.070
MAL	50 ± 6	48 ± 3	0.242
MIS	51 ± 4	51 ± 3	0.744
MI	50 ± 6	45 ± 3	0.009
MIL	50 ± 5	42 ± 6	0.001
M average	51 ± 3	47 ± 2	<0.001
AAS	59 ± 5	50 ± 2	<0.001
AA	59 ± 4	51 ± 3	<0.001
AAL	58 ± 6	53 ± 4	0.012
AIS	56 ± 7	49 ± 3	0.002
AI	56 ± 12	48 ± 2	0.021
AIL	55 ± 11	42 ± 4	<0.001
A average	57 ± 6	49 ± 2	<0.001
Total average	53 ± 3	48 ± 2	<0.001

Table 38: T2 CMRI findings in HFpEF: Events versus no events

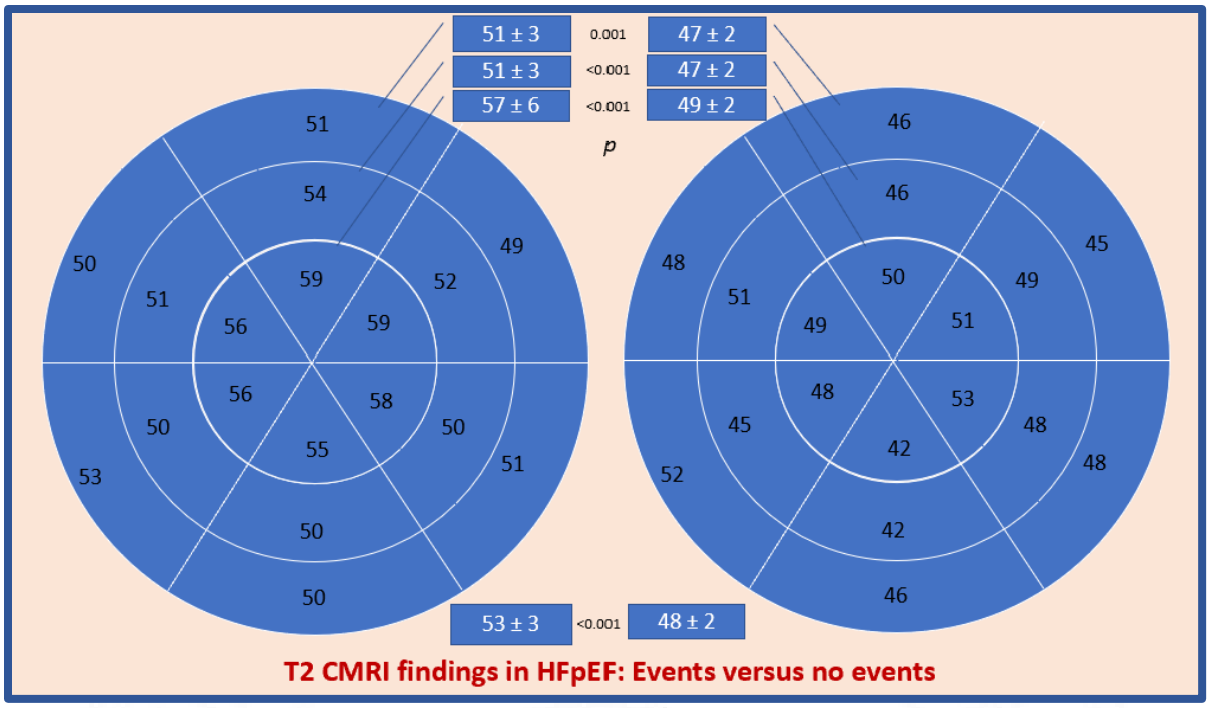


Figure 28: T2 CMRI findings in HFpEF: Events versus no events

There were no significant differences between T1 values regardless of LGE positivity in cases (*p 0.321)*. However LGE negative cases had significantly increased T1 values in all segments compared to healthy control group (Total T1, mean ± SD; 1053 ± 62vs 1020 ± 4, *p* < *0*.001), **(Table 39, 40)**).

	LGE - (N = 22) (mS)	LGE + (N = 8) (mS)	p
Basal T1	1041 ± 63	1052 ± 95	0.354
Mid T1	1053 ± 56	1085 ± 82	0.120
Apical T1	1065 ± 81	1064 ± 106	0.485
Total T1	1053 ± 62	1067 ± 94	0.321

Table 39: T1 CMRI findings in HFpEF: LGE + versus LGE -

	LGE - (N = 22) (mS)	Control (N = 30) (mS)	p
Basal T1	1041 ± 63	1020 ± 5	<0.001
Mid T1	1053 ± 56	1020 ± 8	<0.001
Apical T1	1065 ± 81	1020 ± 4	<0.001
Total T1	1053 ± 62	1020 ± 4	<0.001

Table 40: Distribution of T1 CMRI findings in HFpEF: LGE - versus control

Univariate logistic regression showed that increased BMI, increased cardiothoracic ratio or carinal angle on chest x-ray, increased septal thickness or left ventricular mass index were associated with HFpEF compared to control population. Total T1 value but not T2 was associated with HFpEF compared to control. However multiple logistic regressions did not show any significant association of any of the parameters **(Table 41, Figure 29).**

Variable	**Unadjusted OR (95% Confidence Interval)**	**P**	**Adjusted OR (95% Confidence Interval)**	**P**
BW, kg				
BMI, kg/m^2	1.32 (1.10, 1.58)	0.002		
Saturation in RA, %	0.62 (0.38, 1.01)	0.053		
CTR, %	3.10 (1.50, 6.42)	0.002	3.12 (0.87, 11.15)	0.081
Carinal angle, degree	4.50 (1.66, 12.19)	0.003		
Echocardiography				
LVIDD, mm	1.35 (1.12, 1.63)	0.002		
LVIDS, mm	1.39 (1.14, 1.69)	0.001		
IVS D, mm	9.56 (2.64, 35.34)	0.001		

IVS S, mm	6.84 (2.63, 17.78)	<0.001		
PW D, mm	10.91 (2.83, 42.02)	0.001		
PW S, mm	23.37 (4.12, 132.48)	<0.001		
LV mass [ASE], gm	1.16 (1.06, 1.26)	0.001		
LVMI [ASE], gm/m^2	1.29 (1.07, 1.56)	0.007		
LV mass [Th], gm	1.19 (1.07, 1.33)	0.001		
LVMI [Th], gm/m^2	1.27 (1.09, 1.48)	0.002		
RVID, mm	1.92 (1.30, 2.84)	0.001		
EF, %	0.96 (0.89, 1.03)	0.243		
FS, %	0.92 (0.84, 1.01)	0.083		
LAV, mL	1.57 (1.22, 2.02)	0.001		
LAVI, mL/m2	1.68 (1.24, 2.28)	0.001		
EDT, mS	0.92 (0.88, 0.96)	<0.001		
Lateral E/e’	3.34 (1.67, 6.70)	0.001		
Medial E/e’	1.89 (1.37, 2.61)	<0.001		
Average E/e’	2.31 (1.46, 3.67)	<0.001	10.22 (0.39, 267.22)	0.163
RVSP , mmHg				
TAPSE, mm	0.75 (0.57, 0.99)	0.043		
CMRI				
LVIDD, mm	0.96 (0.86, 1.07)	0.436		
LVIDS, mm	1.07 (0.99, 1.17)	0.105		
IVS D, mm	1.44 (1.10, 1.89)	0.009		
IVS S, mm	1.83 (1.32, 2.55)	<0.001		
PW D, mm	2.45 (1.53, 3.92)	<0.001		
PW S, mm	1.36 (1.12, 1.66)	0.002		
RVID, mm	1.56 (1.23, 1.96)	<0.001		
LV Mass, gm	1.04 (1.01, 1.07)	0.004		
LVMI, gm/m^2	1.05 (1.01, 1.10)	0.010		
LAV, mL	1.24 (1.10, 1.39)	<0.001		
LAVI, mL/m2	1.25 (1.11, 1.40)	<0.001		

LVEDV, mL	1.07 (1.03, 1.11)	<0.001		
LVEDVI, mL/m2	1.09 (1.04, 1.15)	0.001		
LVESV, mL	1.08 (1.02, 1.14)	0.010		
LVESVI, mL/m2	1.11 (1.02, 1.20)	0.018		
LVSV, mL	1.11 (1.05, 1.17)	<0.001		
LVSVI, mL/m2	1.14 (1.06, 1.23)	0.001		
LVCO, L/min	0.86 (0.51, 1.43)	0.552		
LVCOI, L/min/m^2	0.68 (0.31, 1.51)	0.346		
LVEF, %	0.99 (0.92, 1.07)	0.763		
RVEDV, mL	0.97 (0.94, 0.99)	0.009		
RVEDVI, mL/m2	0.92 (0.88, 0.97)	0.002		
RVESV, mL	0.99 (0.96, 1.03)	0.661		
RVESVI, mL/m2	0.97 (0.91, 1.04)	0.362		
RVSV, mL	0.95 (0.92, 0.98)	0.002		
RVSVI, mL/m2	0.90 (0.85, 0.96)	0.001		
RVCO, L/min	0.58 (0.36, 0.94)	0.026		
RVCOI, L/min/m2	0.32 (0.14, 0.72)	0.006		
RVEF, %	0.93 (0.88, 1.00)	0.034		
T1 values (mS)				
Base T1	1.01 (1.00, 1.02)	0.082		
Mid T1	1.04 (1.01, 1.08)	0.010		
Apical T1	1.02 (1.00, 1.03)	0.030		
Total T1	1.02 (1.00, 1.04)	0.029		
T2 values (mS)				
Base T2	0.67 (0.49, 0.91)	0.011		
Mid T2	0.70 (0.53, 0.91)	0.009		
Apical T2	1.19 (0.99, 1.42)	0.066		
Total T2	0.94 (0.77, 1.15)	0.545		

Table 41: Univariate and Multiple logistic regression analysis

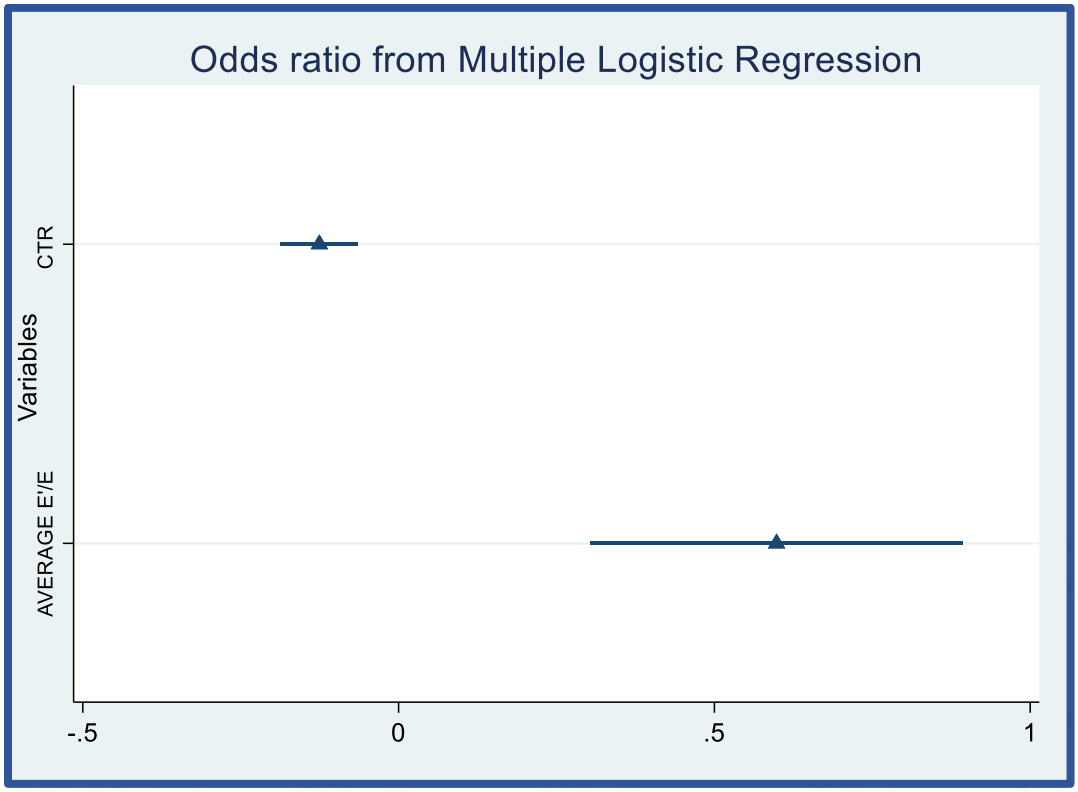


Figure 29: Univariate and Multiple logistic regression analysis

There was moderate positive correlation with MRI derived interventricular septal thickness in diastole and total (Pearson correlation coefficient r = 0.54, $p = 0.002$) and mid-segment average (r = 0.63, $p < 0.001$) T1 value. However there was no strong corelation between left ventricular mass index by MRI. There were no correlation with echocardiography derived interventricular septal thickness, left ventricular mass index with T1 values (**Figure 30, 31, 32, 33**).

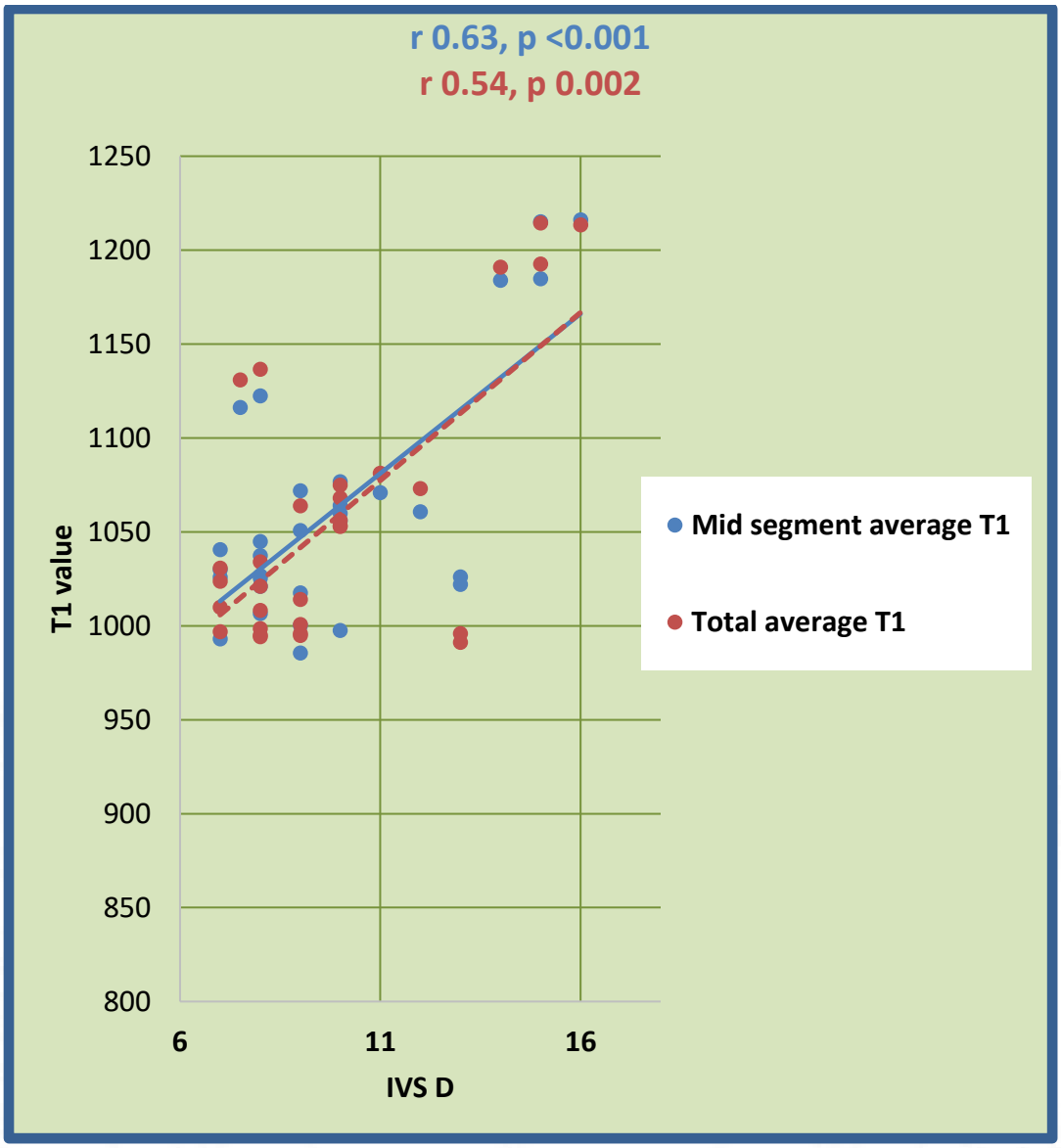


Figure 30: Correlation of T1 value and Inter-ventricular septal thickness in diastole by CMRI

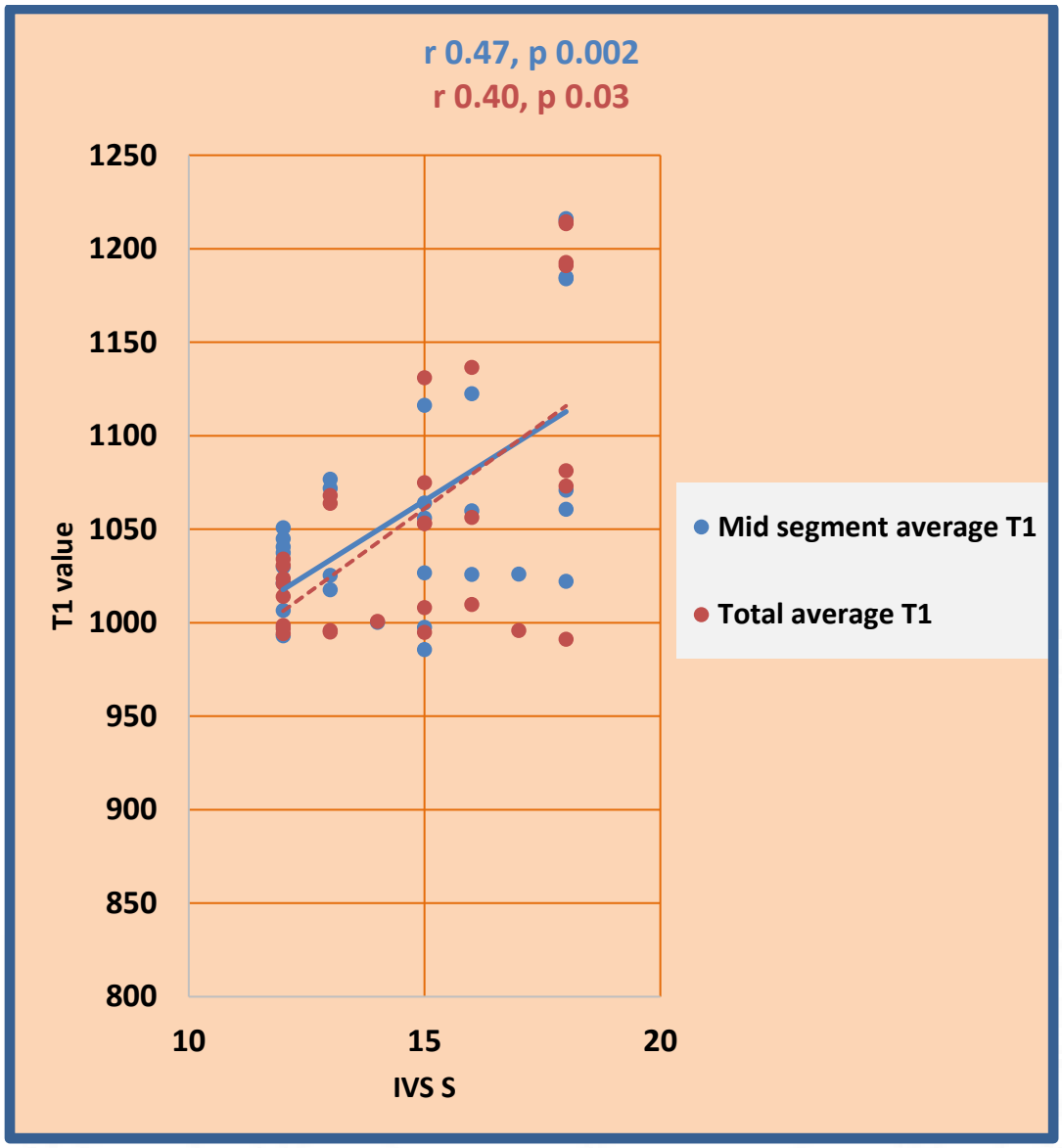


Figure 31. Correlation of T1 value and Inter-ventricular septal thickness in systole by CMRI

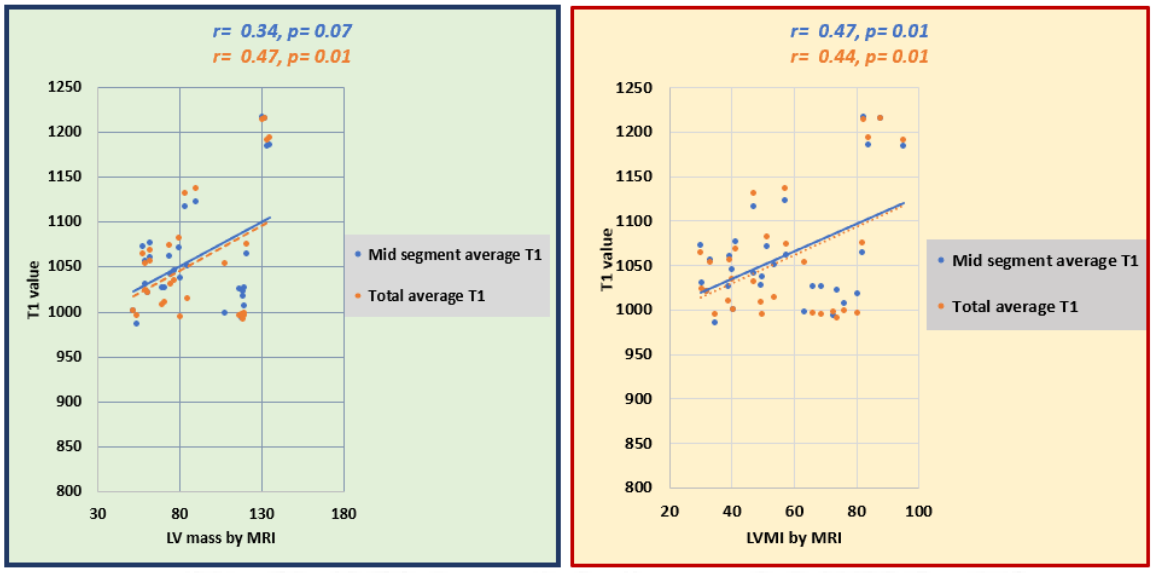
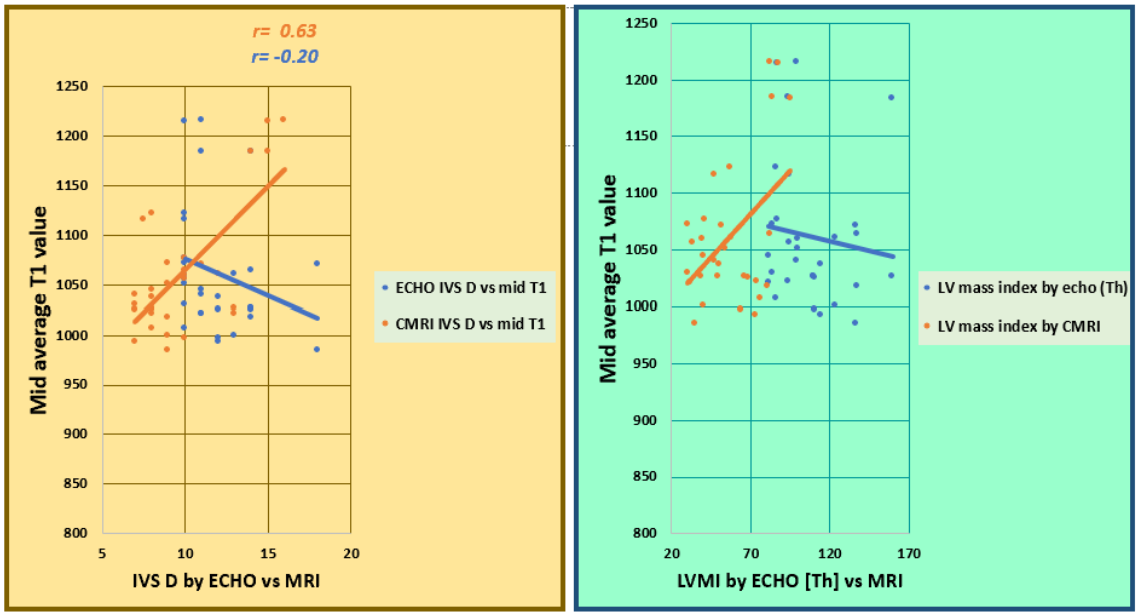


Figure 32, 33: Correlation of T1 value and LV mass and LV mass index by CMRI



(Table 42, Figure 34, 35, 36) T1 value correlation and comparison with interventricular thickness and LV mass index by echocardiography and CMRI

Echocardiogram significantly overestimated interventricular septal (mean difference ± SD, 2.15 ± 1.91 mm) and posterior wall thickness (mean difference ± SD, 2.37 ± 2.11 mm) in diastole,

left ventricular mass index by both ASE (mean difference ± SD, 63 ± 25 gm/m^2) and Teicoltz (mean difference ± SD, 51 ± 21 gm/m^2) formula compared to MRI.

ECHO-MRI	Mean difference	95% CI
LVIDD (mm)	-1.17 ± 4.63	[-2.90, +0.56]
LVIDS (mm)	-1.1 ± 6.10	[-3.38, +1.18]
IVS D (mm)	2.15 ± 1.91	[+1.44, +2.86]
IVS S (mm)	-0.57 ± 2.65	[-1.56, +0.42]
PW D (mm)	2.37 ± 2.11	[+1.58, +3.15]
PW S (mm)	-1.03 ± 3.39	[-2.30, +0.23]
LV mass [ASE-MRI] (gm/m2)	100 ± 37	[86, 114]
LV mass index [ASE-MRI] (gm/m2)	63 ± 25	[53, 72]
LV mass [Th-MRI] (gm/m2)	81 ± 31	[70, 93]
LV mass index [Th-MRI] (gm/m2)	51 ± 21	[43, 59]
LV mass [ASE-Th] (gm/m2)	19 ± 9	[15, 22]
LV mass index [ASE-Th]	12 ± 6	[9, 14]
LAV (mL/m2)	-4.0 ± 15.1	[-9.7, +1.6]
LAVI (mL/m2)	-2.7 ± 9.5	[-6.2, +0.9]

Table 42. Comparison of TTE and CMRI findings

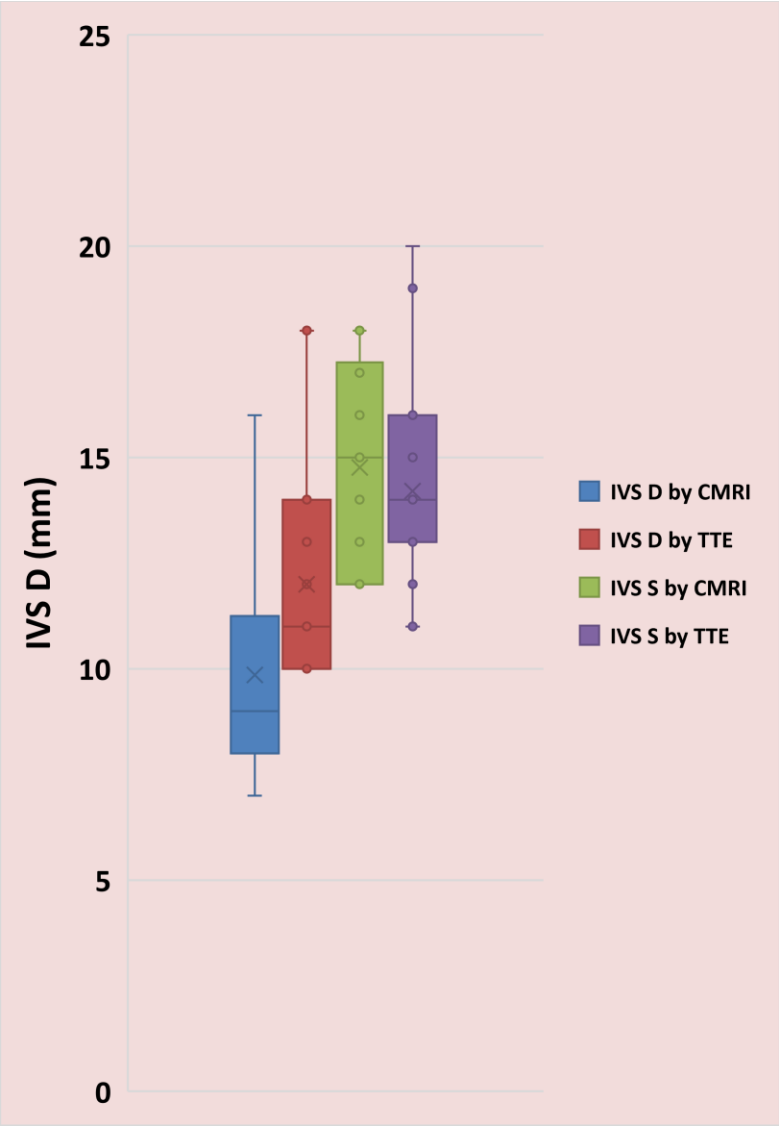


Figure 37: Comparison of inter-ventricular septum (IVS) thickness by transthoracic echocardiography (TTE) and cardiac MRI.

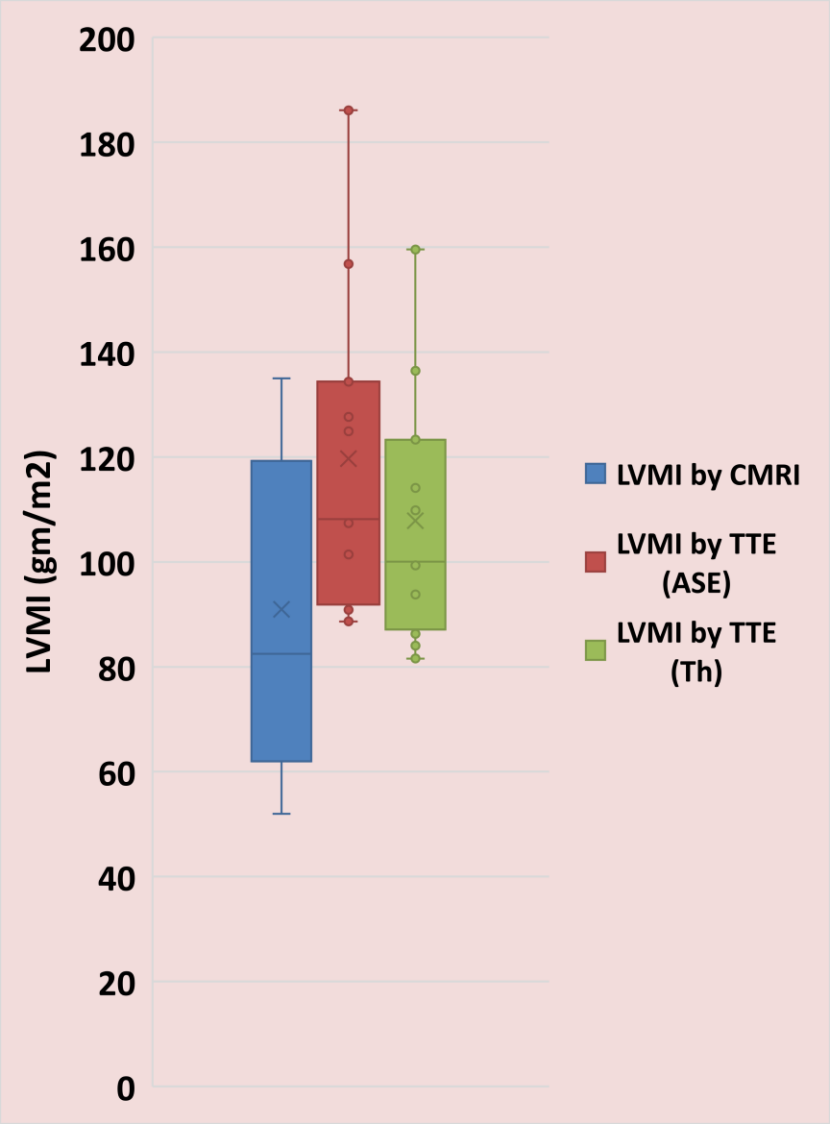


Figure 38: Comparison of left ventricular mass index (LVMI) by transthoracic echocardiography (TTE) ASE and Th formula, and cardiac MRI.

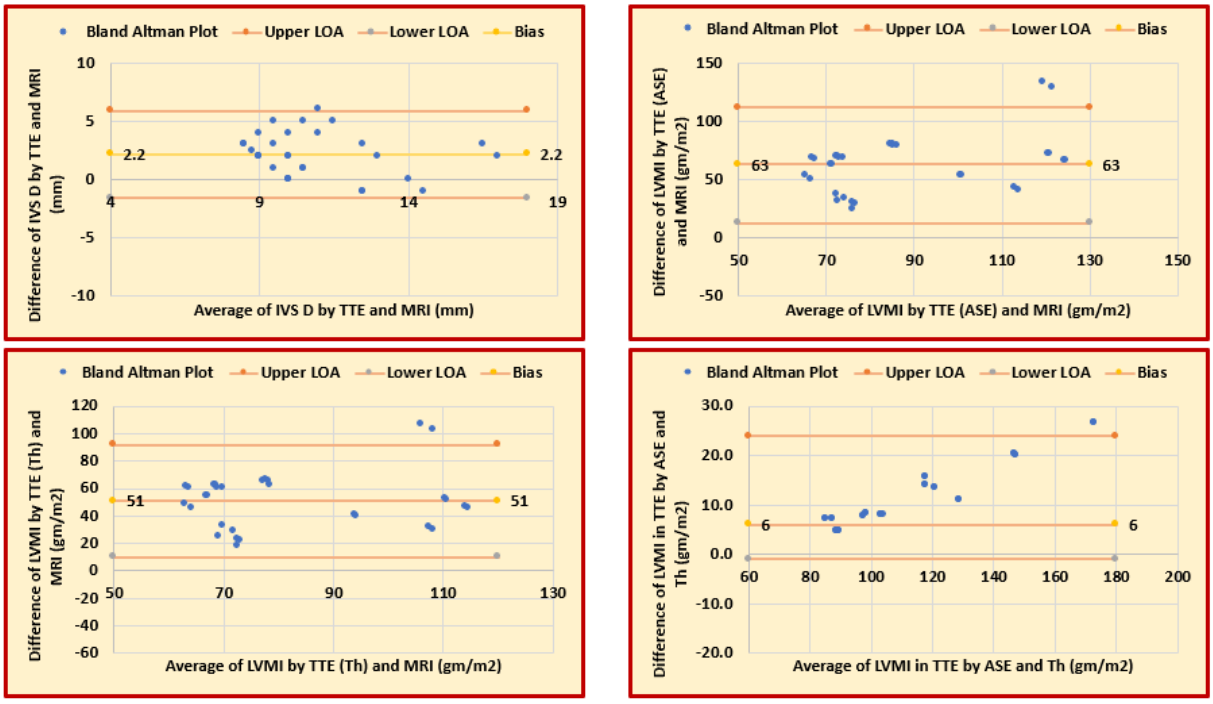


Figure 39: Bland-Altman plots of the mean differences between transthoracic echocardiography (TTE) and cardiac MRI measurements.

Discussion

Discussion

Our study showed that patients with HFpEF are more likely to be female, older and obese, a fact which has been documented by colleagues from around the world. (Andersson and Vasan, 2014; Fonarow et al., 2007) Recent studies have shown that prevalence of obesity among HFpEF subjects can reach up to 95%.(Borlaug et al., 2018) In our experience, hypertension, diabetes and history of coronary artery disease were associated with HFpEF which are known risk factors for development HFpEF.(Borlaug, 2013; Zhao et al., 2022) Although history of COVID-19 infection and obstructive sleep apnea were numerically higher, it did not achieve statistical significance in our study.

Kanagala and colleagues have published their findings in the seminal publication titled Relationship Between Focal and Diffuse Fibrosis Assessed by CMR and Clinical Outcomes in Heart Failure With Preserved Ejection Fraction.(Kanagala et al., 2019) The authors have found that patients with HFpEF had a high burden of obesity, hypertension, diabetes, and atrial fibrillation. On a similar note, Roy et al in 2018 have observed a high prevalence of established cardiovascular risk factors in our HFpEF population; including arterial hypertension (93%), diabetes (39%), hypercholesterolemia (67%), and higher body mass index (BMI).(Roy et al., 2018) Both these publications reflect our finding of metabolic risk factors playing a dominant role in the pathogenesis of HFpEF. Interestingly, in a study titled Evaluation of age-related interstitial myocardial fibrosis with cardiac magnetic resonance contrast-enhanced T1 mapping: MESA (Multi-Ethnic Study of Atherosclerosis), the authors found a weak association between ECV and age.(Liu et al., 2013)

Clinical features in our cases were corroborative of left heart failure with the predominant symptom being breathlessness. Palpitations were the predominant symptom in patients with co-existing atrial fibrillation. Baseline saturation was lower because of inclusion of NYHA functional class IV patients. Murmurs were heard predominantly because of tricuspid regurgitation.

H_2FPEF and HFA-PEFF scoring systems have moderate sensitivity in predicting diagnosis of HFpEF. This has been established from previous studies conducted in the western world. An Italian study titled Value of the HFA-PEFF and H_2FPEF scores in patients with heart failure and

preserved ejection fraction caused by cardiac amyloidosis published in 2022 concluded that the HFA-PEFF score has a higher diagnostic utility in HFpEF caused by CA and holds independent prognostic value for all-cause mortality, while the H_2FPEF score does not.(Tomasoni et al., 2022) All previous studies on these scoring system were framed and validated based on western sub-population studies.(Faxen et al., 2021) Most of the patients in study population were having >5 points, indicating higher than expected probability of clinical diagnosis of HFpEF by those algorithms. This is probably because of difference in patients characteristics in the Asian population compared to western population with HFpEF.

Most of the patients with HFpEF in our study were on ACEi or ARB for control of hypertension. In comparison, lesser number of patients were on SGLT2i which is a class IIa recommendation for treatment of HFpEF as per recent guidelines. The study by Kanagala et al reflects this finding with a maximum number of subjects being on ACEi or ARBs.(Kanagala et al., 2019) In the PARAGON HF trial, the large majority of patients were prescribed angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (85%), β-blockers (80%), calcium channel blockers (36%), and mineralocorticoid receptor antagonists (24%).(Solomon et al., 2018)

We found that 20% of the cases were in atrial fibrillation during presentation which is in coherence with previous studies. Mean QRS duration was higher in cases probably because of inclusion of 6 patients of bundle branch block in the case group. However the prolonged QRS duration might also be explained by the fact that most of the HFpEF patients have subclinical myocardial fibrosis which subtly affects interventricular conduction delay. Although echocardiographic evidence of left ventricular hypertrophy (LVH) was present in most of the patients, electrocardiographic evidence of LVH was very less (13%) in case group probably because of less sensitivity of electrocardiography to diagnose LVH.

Carinal angles were significantly higher in heart failure patients because of significant left atrial dilatation. Carinal angle more than 75 degree is considered abnormal and indicates left atrial dilatation. It is in concordance with a study published in 2010, which proved that the assessment of carinal angle to determine left atrial size was acceptable and repeatable.(Quinton et al., 2010) However, sub-carinal angle measurement and its association has not been reported in previous studies in patients with HFpEF.

Most of the patients in case group had left ventricular hypertrophy by echocardiography probably because of uncontrolled hypertension in almost all of the patients. In our experience, Left ventricular mass index was significantly higher in cases both by Teichholz (mean ± SD; 108 ± 23 vs 70 ± 12) and ASE formula (mean ± SD; 120 ± 29 vs 72 ± 13). Moreover, Left atrial volume was significantly higher in cases which were concordant with previous studies on heart failure with preserved ejection fraction. In the study by Roy et al, compared to age- and sex-matched healthy controls, HFpEF patients had higher E/e' ratio, higher indexed LA and RA volumes, higher RV/RA gradient, and worse RV function as evaluated by TAPSE and FAC. (Roy et al., 2018)

Left ventricular mass using ASE formula was estimated significantly higher compared to Teichholz formula. This is because additional multiplication factor in Teichholz formula and multiple studies have shown that Teichholz formula fares better than ASE formula in terms of MRI derived cardiac mass.

MRI is considered the gold-standard for anatomical measurements of cardiac chambers and walls. In accordance to the echocardiographic finding interventricular septal thickness and posterior wall were higher because of concentric LVH. Left ventricular end diastolic and stroke volume were higher in case group which was probably because of associated mitral regurgitation.

Although left ventricular cardiac output was similar in both the groups, right ventricular forward cardiac output was lower among our cases. Presence of tricuspid regurgitation might have contributed to a diminution in forward output of the right ventricle, in case group.

MRI derived right ventricular volume was lower in cases probably because of septal hypertrophy reducing effective right ventricular volume and partly contributed by mildly increased right ventricular systolic pressure because of mild pulmonary hypertension in most of the cases.

Average mid-segment and total average T1 native values were significantly higher in cases which have also been proven in various studies. T1 has been proven to be associated and correlated with histology proven myocardial fibrosis. However a surrogate marker of myocardial fibrosis is extra-cellular volume (ECV) which has shown marked promise in predicting

myocardial fibrosis and clinical outcomes.(Golukhova et al., 2022; Kanagala et al., 2019; Roy et al., 2018)

Cumulative event was 67% in our cases over a mean follow up of 25 months which was similar to most of the outcome studies in heart failure with preserved ejection fraction. Mortality was 7% which was lower compared to previous studies which was probably due to exclusion criteria of our study which excluded patients with disease with worse outcomes like amyloidosis, restrictive cardiomyopathy and coronary artery disease.

Both the event and no-event groups had uncontrolled hypertension which was reflected as LVH. NT-pro-BNP was significantly higher in event group indicating this group to be sicker and explaining its relation with subsequent events. Previous studies also showed the relationship with recurrent heart failure hospitalization and major adverse cardiovascular events.

Frusemide and MRA requirement was higher in event group indicating that this group was decompensated and sick requiring multiple medication and decongestion.

Carinal angle and left atrial enlargement were higher in event group due to left atrial enlargement. There were no significant differences in echocardiographic parameters between event and no-event group probably indicating lesser sensitivity of echocardiography in predicting a major adverse cardiovascular event. Pericardial effusion was exclusively present in event group indicating elevated central venous pressure in sicker patients.

Interventricular septum and posterior wall thickness were higher in event group compared to no-event group. Previous studies had also proven the fact that increased severity hypertrophy, increased cardiac mass are associated with increased event of incident and recurrent heart failure as well as mortality.

Focal fibrosis in the form LGE was significantly higher in HFpEF population with none being affected in control group. However there were no significant differences in event and no-event group which is in-contrary to the most of the studies involving HFrEF, hypertrophic cardiomyopathy patients. However Kanagala et al also had reported similar result and attributed the difference in result to the technique for LGE measurements.(Kanagala et al., 2019)

Our study focused on native T1 value and it reflects intra and extracellular changes. T1 value was significantly increased in event group compared to no-event group in our study population. Recent meta-analysis showed ECV (a surrogate marker of T1) rather than T1 is more predictive of adverse outcome in HFpEF patients. However all previous studies included western population and very diverse phenotypes of HFpEF population. Our study was first in south-Asian country where we included "pure" HFpEF patients and excluded all coronary artery disease, hypertrophic cardiomyopathy and amyloidosis patient which have different prognosis and different therapeutic interventions. This is why probably our patients' T1 value came out to be predictive of events. However further larger studies are required to validate the continental difference in MRI findings.

We also found that LGE negative patients had significantly higher T1 values compared to control indicating sensitivity of detecting HFpEF patients by higher T1 remains even in absence of LGE.

In univariate logistic regression model T1 was predictive of HFpEF compared to control. However in multivariate analysis only cardiothoracic ratio and average E/e' could be analyzed which were not significant. The reason why only two variables were considered for multivariable regression is because adding other variables did not improve the model further. By the method of conditional forward selection procedure, these two variables were selected to adhere by the principle of parsimony.

T1 values were fairly seen to be correlated with interventricular septal thickness by MRI but not by echocardiogram. This is probably due to variability of echocardiographic measurements and intrinsic errors involved in it. Previous studies also had shown that echocardiogram can significantly overestimate myocardial thickness measurements compared to gold-standard MRI in patients with hypertrophic cardiomyopathy, Fabry's disease.(Hindieh et al., 2017; O'Brien et al., 2020)

We found that left ventricular mass index and septal thickness were significantly overestimated in echocardiogram. This was also consistent with previous studies. Overestimation is likely due to geometric assumption of left ventricle as prolate ellipsoid and symmetrical distribution of left ventricular hypertrophy which are not the case in most of the times. However error was higher in

our study probably because of inclusion of epicardial fat in the measurement as most of the patients were obese and were having epicardial fat.

Summary and Conclusions

Conclusions

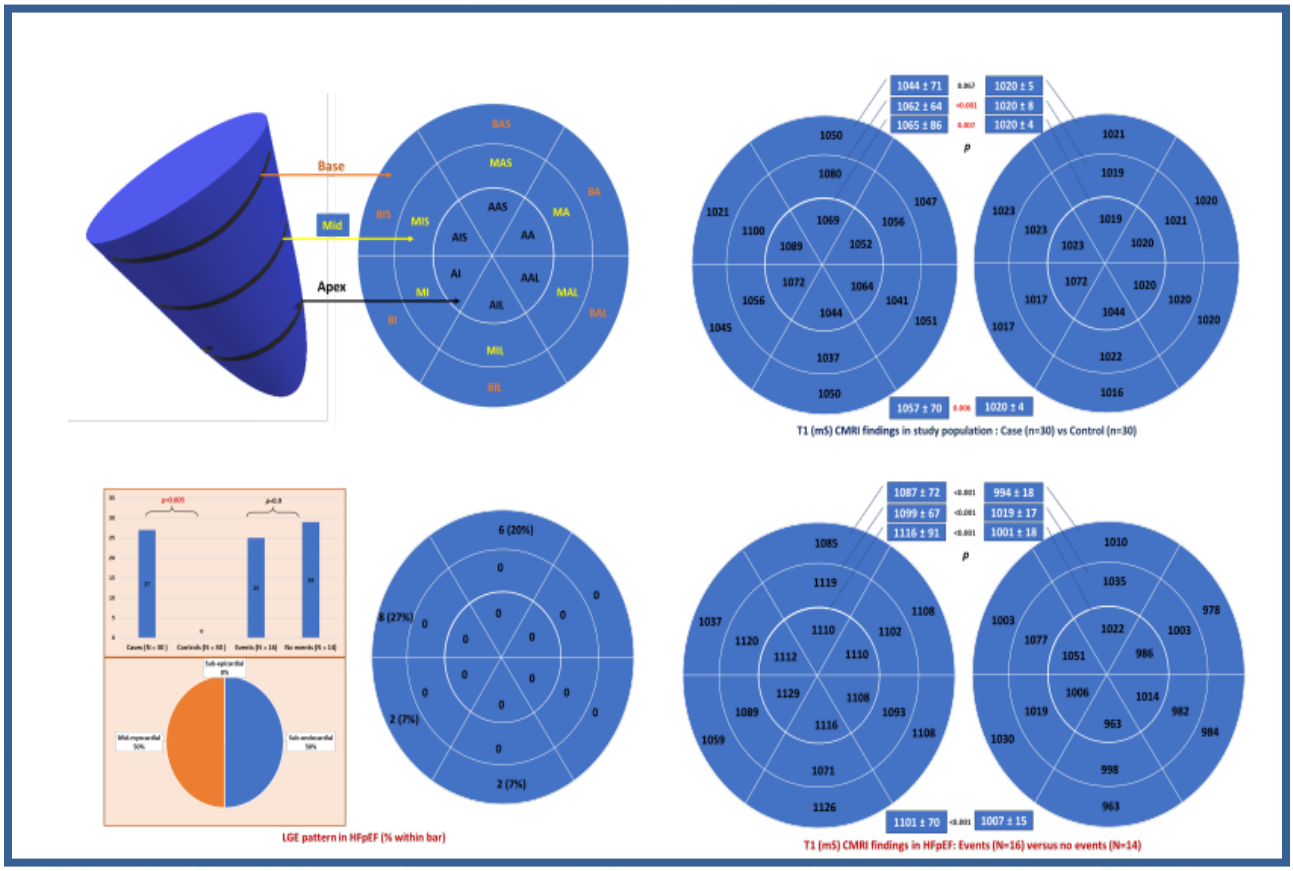
The conclusions from this study include:

1. A higher age, the female gender, obesity, diabetes, hypertension and dyslipidemia are strong predictors of HFpEF
2. Higher respiratory rate, lower oxygen saturation and presence of pedal edema are associated with HFpEF
3. Electrocardiographic findings of left atrial enlargement, left ventricular hypertrophy, leftward QRS axis, higher QRS duration and higher QTc are associated with HFpEF
4. Radiological cardiac enlargement and left atrial enlargement are associated with HFpEF
5. On Echocardiography , higher Mean inter-ventricular septal thickness in diastole and systole, higher left ventricular posterior wall thickness in diastole and systole, higher Left ventricular mass index, higher Right ventricular internal diameter and higher Left atrial volume index are associated with HFpEF.
6. On Echocardiography, lower Mitral E velocity deceleration time and significantly higher Average E/e' are associated with HFpEF
7. On CMRI, Higher IVS thickness in diastole and systole, higher posterior wall thickness in diastole and systole and higher Left atrial volume index were all associated with HFpEF.
8. On CMRI, Higher Left ventricular mass index, higher left ventricular end diastolic volume index, higher Left ventricular end systolic volume index are all associated with HFpEF but not the LVEF.
9. Lower right ventricular cardiac output, lower Right ventricular end diastolic volume index, lower right ventricular stroke volume index and lower right ventricular ejection fraction on CMRI were predictive of HFpEF

10. Higher baseline heart rate, higher respiratory rate, lower saturation in room air, higher prevalence of elevated jugular venous pressure and gallop rhythm at presentation predicts adverse events in HFpEF
11. Higher NT-Pro-BNP at presentation predicts adverse events in HFpEF
12. Cardiac enlargement and left atrial enlargement are both associated with adverse events in HFpEF
13. Mild pericardial effusion in Echocardiography is associated with adverse events in HFpEF
14. Cardiac catheterization fails to identify patients of HFpEF who are at higher risk of adverse events
15. Higher diastolic IVS and PW thickness are associated with adverse events in HFpEF
16. Lower LVEF and RVEF are associated with adverse events in HFpEF
17. Focal fibrosis as evident by LGE is significantly more in HFpEF.
18. Diffuse fibrosis as evident by increased myocardial native T1 value is significantly high in HFpEF.
19. T2 value is not significantly elevated in HFpEF.
20. Elevated myocardial native T1 is predictive of major adverse cardiac events.
21. Diffuse fibrosis was more prevalent in HFpEF than focal fibrosis.
22. LGE is not predictive of adverse events in HFpEF
23. Higher T1 values are associated with adverse events in HFpEF

Presence of Myocardial Fibrosis on Cardiac MRI and Its Impact on Short-Term Outcomes in an Asian Cohort of Heart Failure with Preserved Ejection Fraction

Structured Graphical abstract:



- **Key Question**

The present study sought to decipher whether there were differences between the presence and extent of both focal and diffuse fibrosis in HFpEF subjects and those in matched control subjects without heart failure and to determine whether fibrosis provided additional prognostic value beyond conventional clinical and echocardiographic indices.

- **Key Finding**

LGE (27% vs 0%, $p = 0.005$) and mid-segment (mean ± SD; 1062 ± 64 vs 1020 ± 8, $p < 0.001$) T1 values were significantly higher in the HFpEF group compared to the control group. Moreover, average mid-segment (mean ± SD; 1099 ± 67 vs 1019 ± 17, $p < 0.001$) T1 values were significantly higher in the event group compared to no-event.

- **Take-home Message**

Higher T1 but not T2 was associated with the HFpEF group compared to the age and sex-matched control group. Focal fibrosis as evident by LGE is significantly more in HFpEF. Among HFpEF patients, high T1 myocardial values were associated with a higher rate of all-cause death, stroke, and HF hospitalization in short-term follow-up.

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Annexures

Biodata of Dr Sudipta Mondal, DM Trainee

Sudipta	**Mondal**	
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Academic Qualifications (Most recent qualification first)

Degree/Certificate	Year	Institution, Country
DNB General Medicine	2019	NBE, New Delhi
MD General Medicine	2019	The West Bengal University of Health Sciences, Kolkata
MBBS	2014	The West Bengal University of Health Sciences, Kolkata

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration

TC MC Reg : 80886, dated 10.09.2021

West Bengal Medical Council: 73195, dated 30.06.2015

Current and previous positions (most recent position first)

Month and Year	Title	Institution/Company, Country
January 2021	**SR, DM Cardiology course**	SCTIMST, Trivandrum, Kerala
June 2019	**SR, Medicine**	Murshidabad MC, Berhampore, WB
May 2016	**JR, Medicine**	North Bengal Medical College, Darjeeling, WB

Brief summary of relevant research experience:

1. Epidemiological Review and Sensitivity Patterns of CBNAAT Testing for Tuberculosis in a Teaching Hospital of Eastern India. **JIMA** 2020;18(12):43-48.
2. Etiological study of seizure disorders among patients attending the epilepsy clinic of an urban center in Eastern India. **JIMA** 2020;18(7):43-45.
3. Establishing Normal Echocardiographic Measurements In Healthy Indian Newborn Infants. **Asia Pac J Paediatr Child Health** 2021;4:11-17.

Current project/s at hand

Signature Sudipta Mondal	Date: Place: SCTIMST, Trivandrum, Kerala

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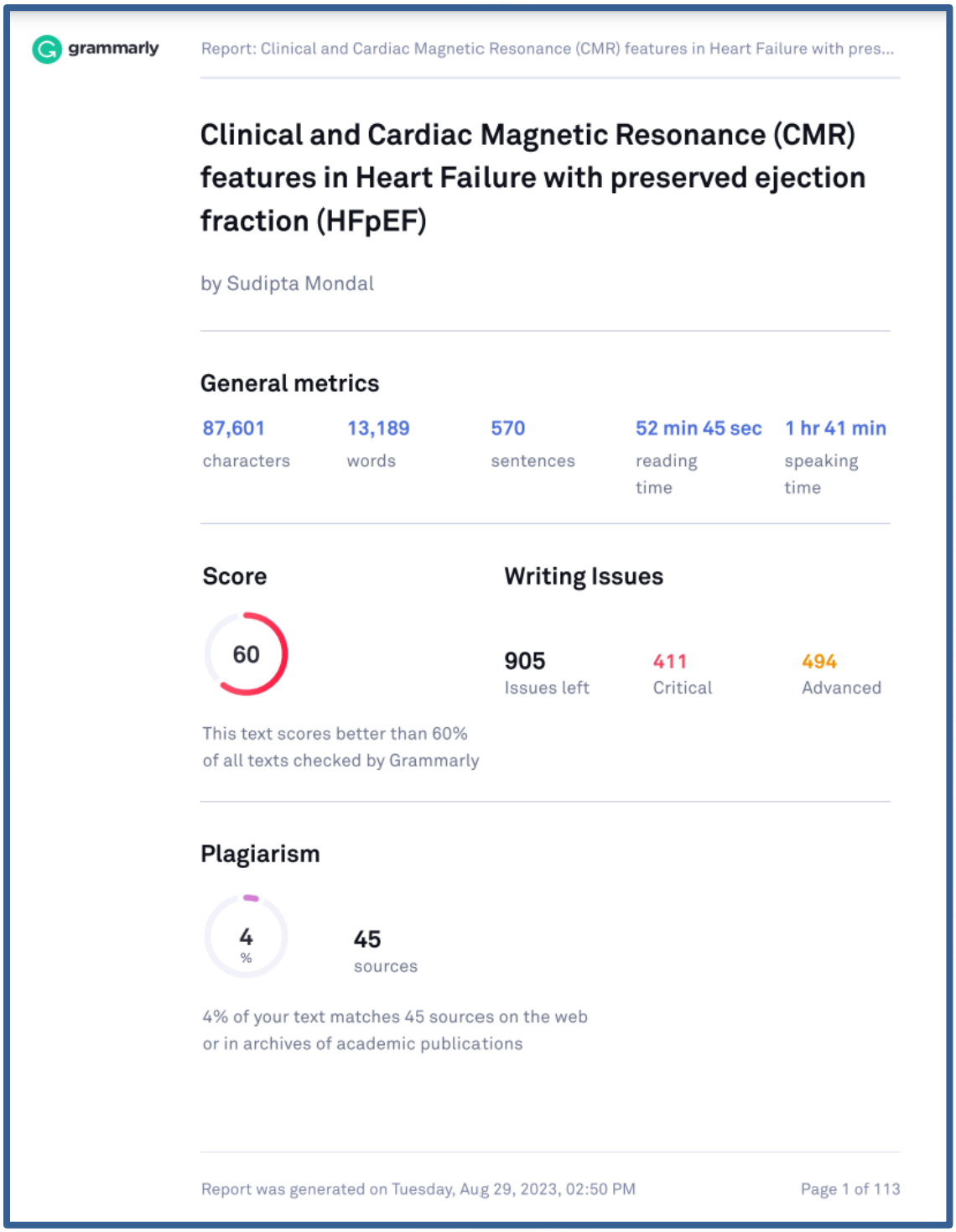

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Report: Clinical and Cardiac Magnetic Resonance (CMR) features in Heart Failure with pres...

Clinical and Cardiac Magnetic Resonance (CMR) features in Heart Failure with preserved ejection fraction (HFpEF)

by Sudipta Mondal

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Proforma

Clinical and Cardiac Magnetic Resonance (CMR) features in Heart Failure with preserved ejection fraction (HFpEF): Case Record Form

Serial No. **Date of clinical presentation:** **Date of CMR:**

Demographic data									
Age	**Sex**	**Height (cm)**	**Weight (kg)**	**BMI**	**HTN**	**DM**	**COPD**	**CAD**	**Dyslipid**
Clinical features and significant past history:									
Echocardiographic data									
CMR data									
LV	**IVSd**	**LVPWd**	**LV mass**	**LV Mass index**	**Wall motion**				
LV	**ED volume**	**ED volume index**	**ES volume**	**ES volume index**	**Stroke volume**	**Stroke volume index**	**Cardiac output**	**Cardiac output index**	**Ejection fraction**
RV	**ED volume**	**ED volume index**	**ES volume**	**ES volume index**	**Stroke volume**	**Stroke volume index**	**Cardiac output**	**Cardiac output index**	**Ejection fraction**
LVOT and Aortic root									
LA	**RA**	**Edema, inflammation and diffuse fibrosis**							
Perfusion					**Delayed enhancement**				

Valves and pericardium	**Others**
Final CMR comments:	
Complete diagnosis	

Signature

Annexure

Information sheet for study participants

TITLE OF THE STUDY: Clinical and Cardiac Magnetic Resonance (CMR) features in Heart Failure with preserved ejection fraction (HFpEF)

SERIAL NUMBER: Name of the participant:
Gender: Date of birth: Age in years:

Study background: The heart functions as a pump to supply oxygen and nutrition carrying blood to the tissues. Heart failure is a disease in which the heart is unable to pump blood adequately. Heart failure with preserved ejection fraction is a special type of heart failure where this heart failure may be associated with other diseases like diabetes, asthma or even obesity. You have been informed that you / your patient has been suffering from heart failure with preserved ejection fraction, for which he / she has already undergone several tests. Cardiac MRI is a sophisticated test available at Sree Chitra Institute for Medical Sciences and Technology which is being used across the world for a better and more detailed understanding of the heart in patients with heart failure.
You are being asked to participate in a study where selected patients of Heart Failure with preserved Ejection Fraction will be asked to undergo this sophisticated investigation. Participating in this study will allow the medical team to use information like your / your patient's medical history and results of all investigations performed, but will not affect the treatment in any way.

What is Heart Failure with preserved Ejection Fraction: Heart failure is a clinical condition where the pumping action of the heart is inadequate for normal function of the body. This can be due to disease of the heart or due to other conditions. Ejection fraction is a finding that is established from echocardiography, a test routinely performed for heart failure. Patients with heart failure may have reduced ejection fraction or preserved ejection fraction, depending on their disease.

What is meant by clinical features: Clinical features mean that we would study parameters like age of the patient, symptoms and signs of the disease, past medical history and response to treatment.
What is **Cardiac Magnetic Resonance:** Cardiac Magnetic Resonance is a sophisticated investigation that is recently being used to better understand the condition of the heart in various diseases, like heart failure. It is performed with a MRI machine and produces images or pictures like an X-ray or CT scan machine. No injection or other medicines are administered in

CMR and there is no pain to the patient. However, the investigation takes a long time (around 60 – 70 minutes) and the patient needs to lie quietly inside the machine.

Does it involve any interventional procedure? No. As already mentioned, CMR will not involve any interventions in the form of medicines, operation or injections

If you take part what will you have to do? Participating in this study will not involve any extra treatment procedures or duration of hospitalization. Only if your doctor is prescribing CMR for heart failure with preserved ejection fraction will you be requested to participate in this study. The usual cost of treatment, including the cost of CMR will need to be borne by you. No additional cost will be incurred and no additional drugs will be given to you.

Can you withdraw from this study after it starts? Yes. Your participation in this study is entirely voluntary and you are free to withdraw permission to participate from the study. If you do so, it will not affect your usual treatment at this hospital, including your eligibility for Cardiac Magnetic Resonance study.

Whether there is any risk related to this study? There is no individual risk or benefit to the patient as this is an observational study.

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 the study.

If at any time you experience any problems or you have any further questions, you are free to contact:

1. **Dr Sudipta Mondal**, Principal Investigator (sudiptamondalnrs@gmail.com, 7686906481) or
2. **Dr. Srinivas G**, Member Secretary, Institutional Ethical Committee, SCTIMST, Thiruvananthapuram

Annexure

अध्ययन प्रतिभागियों के लिए सूचना पत्र

अध्ययन का शीर्षक: क्लिनिकल और कार्डिएक मैग्नेटिक रेजोनेंस (CMR) हार्ट फेल्योर में संरक्षित इजेक्शन अंश (HFpEF) के साथ सुविधाएँ

क्रमिक संख्या: प्रतिभागी का नाम:

लिंग: जन्म की तारीख: आयु वर्षों में:

अध्ययन पृष्ठभूमि: हृदय ऊतकों को रक्त ले जाने वाले ऑक्सीजन और पोषण की आपूर्ति करने के लिए एक पंप के रूप में कार्य करता है। दिल की विफलता एक ऐसी बीमारी है जिसमें हृदय पर्याप्त रूप से रक्त पंप करने में असमर्थ होता है। संरक्षित इजेक्शन अंश के साथ दिल की विफलता एक विशेष प्रकार की हृदय विफलता है जहां यह हृदय विफलता मधुमेह, अस्थमा या मोटापे जैसी अन्य बीमारियों से जुड़ी हो सकती है। आपको सूचित किया गया है कि आप/आपके रोगी को संरक्षित इजेक्शन अंश के साथ दिल की विफलता से पीड़ित किया गया है, जिसके लिए वह पहले से ही कई परीक्षणों से गुजर चुका है। कार्डिएक एमआरआई श्री चित्रा इंस्टीट्यूट फॉर मेडिकल साइंसेज एंड टेक्नोलॉजी में उपलब्ध एक परिष्कृत परीक्षण है जिसका उपयोग हृदय की विफलता के रोगियों में हृदय की बेहतर और अधिक विस्तृत समझ के लिए दुनिया भर में किया जा रहा है।

आपको एक अध्ययन में भाग लेने के लिए कहा जा रहा है जहां संरक्षित इजेक्शन फ्रैक्शन वाले हार्ट फेल्योर के चयनित रोगियों को इस परिष्कृत जांच से गुजरने के लिए कहा जाएगा। इस अध्ययन में भाग लेने से चिकित्सा टीम आपके/आपके रोगी के चिकित्सा इतिहास और की गई सभी जांचों के परिणामों जैसी जानकारी का उपयोग कर सकेगी, लेकिन किसी भी तरह से उपचार को प्रभावित नहीं करेगी।

संरक्षित इजेक्शन फ्रैक्शन के साथ दिल की विफलता क्या है: दिल की विफलता एक नैदानिक स्थिति है जहां हृदय की पंपिंग क्रिया शरीर के सामान्य कार्य के लिए अपर्याप्त होती है। यह हृदय रोग या अन्य स्थितियों के कारण हो सकता है। इजेक्शन फ्रैक्शन एक ऐसी खोज है जो इकोकार्डियोग्राफी से स्थापित होती है, जो दिल की विफलता के लिए नियमित रूप से किया जाने वाला एक परीक्षण है। दिल की विफलता वाले मरीजों में उनकी बीमारी के आधार पर इजेक्शन अंश या संरक्षित इजेक्शन अंश कम हो सकता है।

क्लिनिकल फीचर्स का क्या मतलब है: क्लिनिकल फीचर्स का मतलब है कि हम रोगी की उम्र, बीमारी के लक्षण और लक्षण, पिछले चिकित्सा इतिहास और उपचार के प्रति प्रतिक्रिया जैसे मापदंडों का अध्ययन करेंगे।

कार्डिएक मैग्नेटिक रेजोनेंस क्या है: कार्डिएक मैग्नेटिक रेजोनेंस एक परिष्कृत जांच है जिसका उपयोग हाल ही में हृदय की विफलता जैसे विभिन्न रोगों में हृदय की स्थिति को बेहतर ढंग से समझने के लिए किया जा रहा है। यह एक एमआरआई मशीन के साथ किया जाता है और एक्स-रे या सीटी स्कैन मशीन जैसी छवियां या चित्र तैयार

करता है। सीएमआर में कोई इंजेक्शन या अन्य दवा नहीं दी जाती है और रोगी को कोई दर्द नहीं होता है। हालांकि, जांच में लंबा समय लगता है (लगभग 60-70 मिनट) और मरीज को मशीन के अंदर चुपचाप लेटने की जरूरत होती है।

क्या इसमें कोई हस्तक्षेप प्रक्रिया शामिल है? नहीं। जैसा कि पहले ही उल्लेख किया गया है, सीएमआर में दवाओं, ऑपरेशन या इंजेक्शन के रूप में कोई हस्तक्षेप शामिल नहीं होगा

अगर आप हिस्सा लेंगे तो आपको क्या करना होगा? इस अध्ययन में भाग लेने के लिए कोई अतिरिक्त उपचार प्रक्रिया या अस्पताल में भर्ती होने की अवधि शामिल नहीं होगी। केवल अगर आपका डॉक्टर सीएमआर को दिल की विफलता के लिए संरक्षित इजेक्शन अंश के साथ निर्धारित कर रहा है, तो आपसे इस अध्ययन में भाग लेने का अनुरोध किया जाएगा। सीएमआर की लागत सहित उपचार की सामान्य लागत आपको वहन करनी होगी। कोई अतिरिक्त खर्च नहीं किया जाएगा और आपको कोई अतिरिक्त दवा नहीं दी जाएगी।

क्या आप इस अध्ययन के शुरू होने के बाद इससे पीछे हट सकते हैं? हां। इस अध्ययन में आपकी भागीदारी पूरी तरह से स्वैच्छिक है और आप अध्ययन से भाग लेने की अनुमति वापस लेने के लिए स्वतंत्र हैं। यदि आप ऐसा करते हैं, तो यह इस अस्पताल में आपके सामान्य उपचार को प्रभावित नहीं करेगा, जिसमें कार्डिएक मैग्नेटिक रेजोनेंस अध्ययन के लिए आपकी पात्रता भी शामिल है।

क्या इस अध्ययन से संबंधित कोई जोखिम है? रोगी को कोई व्यक्तिगत जोखिम या लाभ नहीं है क्योंकि यह एक अवलोकन अध्ययन है।

क्या आपकी व्यक्तिगत जानकारी गोपनीय रखी जाएगी? इस अध्ययन के परिणाम एक मेडिकल जर्नल में प्रकाशित किए जाएंगे लेकिन किसी प्रकाशन या परिणामों की प्रस्तुति में आपकी पहचान किसी नाम से नहीं की जाएगी। हालांकि, यदि आप अध्ययन में भाग लेने का निर्णय लेते हैं तो आपकी अतिरिक्त अनुमति के बिना अध्ययन से जुड़े लोग आपके मेडिकल नोट्स की समीक्षा कर सकते हैं।

यदि किसी भी समय आपको कोई समस्या आती है या आपके कोई और प्रश्न हैं, तो आप संपर्क करने के लिए स्वतंत्र हैं:

1. डॉ सुदीप्त मंडल, प्रधान अन्वेषक
(sudiptamondalnrs@gmail.com, 7686906481) या

2. डॉ. श्रीनिवास जी, सदस्य सचिव, संस्थागत नैतिक समिति, एससीटीआईएमएसटी, तिरुवनंतपुरम

Annexure

പഠനത്തിൽ പങ്കെടുക്കുന്നവർക്കുള്ള വിവര ഷീറ്റ്

പഠനത്തിന്റെ ശീർഷകം: സംരക്ഷിത എജക്ഷൻ ഫ്രാക്ഷൻ (എച്ച്എഫ് പിഇഎഫ്) ഉള്ള ഹാർട്ട് പരാജയത്തിലെ ക്ലിനിക്കൽ, കാർഡിയാക് മാഗ്നെറ്റിക് റെസൊണൻസ് (സിഎംആർ) സവിശേഷതകൾ

സീരിയൽ നമ്പർ: പങ്കെടുക്കുന്നയാളുടെ പേര് :

ലിംഗഭേദം: ജനനത്തീയതി:

വർഷങ്ങളിലെ പ്രായം :

പഠന പശ്ചാത്തലം: ടിഷ്യൂകളിലേക്ക് രക്തം എത്തിക്കുന്ന ഓക്സിജനും പോഷണവും നൽകാനുള്ള ഒരു പമ്പായി ഹൃദയം പ്രവർത്തിക്കുന്നു. ഹൃദയത്തിന് വേണ്ടത്ര രക്തം പമ്പ് ചെയ്യാൻ കഴിയാത്ത ഒരു രോഗമാണ് ഹാർട്ട് പരാജയം. പ്രമേഹം, ആസ്ത്മ അല്ലെങ്കിൽ അമിതവണ്ണം തുടങ്ങിയ മറ്റ് രോഗങ്ങളുമായി ഈ ഹൃദയസ്തംഭനം ബന്ധപ്പെട്ടിരിക്കാവുന്ന ഒരു പ്രത്യേക തരം ഹൃദയസ്തംഭനമാണ് സംരക്ഷിത എജക്ഷൻ ഭിന്നസംഖ്യയുള്ള ഹൃദയസ്തംഭനം. സംരക്ഷിത എജക്ഷൻ ഭിന്നസംഖ്യ ഉപയോഗിച്ച് നിങ്ങൾ / നിങ്ങളുടെ രോഗി ഹൃദയസ്തംഭനം അനുഭവിക്കുന്നുണ്ടെന്ന് നിങ്ങളെ അറിയിച്ചിട്ടുണ്ട്, ഇതിനായി അവൻ / അവൾ ഇതിനകം നിരവധി പരിശോധനകൾക്ക് വിധേയമായിട്ടുണ്ട്. ഹൃദയസ്തംഭനമുള്ള രോഗികളിൽ ഹൃദയത്തെക്കുറിച്ച് മികച്ചതും വിശദവുമായ ധാരണയ്ക്കായി ലോകമെമ്പാടും ഉപയോഗിക്കുന്ന ശ്രീ ചിത്ര ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആൻഡ് ടെക്നോളജിയിൽ ലഭ്യമായ ഒരു നൂതന പരീക്ഷണമാണ് കാർഡിയാക് എംആർഐ.

സംരക്ഷിത എജക്ഷൻ ഭിന്നസംഖ്യയുള്ള ഹാർട്ട് പരാജയം തിരഞ്ഞെടുത്ത രോഗികളോട് ഈ സങ്കീർണ്ണമായ അന്വേഷണത്തിന് വിധേയരാകാൻ ആവശ്യപ്പെടുന്ന ഒരു പഠനത്തിൽ പങ്കെടുക്കാൻ നിങ്ങളോട് ആവശ്യപ്പെടുന്നു. ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നത് നിങ്ങളുടെ / നിങ്ങളുടെ രോഗിയുടെ മെഡിക്കൽ ചരിത്രം, നടത്തിയ എല്ലാ അന്വേഷണങ്ങളുടെയും ഫലങ്ങൾ എന്നിവ പോലുള്ള വിവരങ്ങൾ ഉപയോഗിക്കാൻ മെഡിക്കൽ ടീമിനെ അനുവദിക്കും, പക്ഷേ ഇത് ചികിത്സയെ ഒരു തരത്തിലും ബാധിക്കില്ല.

സംരക്ഷിത എജക്ഷൻ ഭിന്നസംഖ്യയുള്ള ഹൃദയ പരാജയം എന്താണ്: ഹൃദയത്തിന്റെ പമ്പിംഗ് പ്രവർത്തനം ശരീരത്തിന്റെ സാധാരണ പ്രവർത്തനത്തിന് അപര്യാപ്തമാകുന്ന ഒരു ക്ലിനിക്കൽ അവസ്ഥയാണ് ഹാർട്ട് പരാജയം. ഇത് ഹൃദയ സംബന്ധമായ അസുഖങ്ങൾ മൂലമോ മറ്റ് അവസ്ഥകൾ മൂലമോ ആകാം. ഹൃദയസ്തംഭനത്തിനായി പതിവായി നടത്തുന്ന ഒരു

പരീക്ഷണമായ എക്കോകാർഡിയോഗ്രാഫിയിൽ നിന്ന് സ്ഥാപിതമായ ഒരു കണ്ടെത്തലാണ് എജക്ഷൻ ഫ്രാക്ഷൻ. ഹൃദയസ്തംഭനമുള്ള രോഗികൾക്ക് അവരുടെ രോഗത്തെ ആശ്രയിച്ച് എജക്ഷൻ ഭിന്നസംഖ്യ അല്ലെങ്കിൽ സംരക്ഷിത എജക്ഷൻ ഭിന്നസംഖ്യ കുറച്ചിരിക്കാം.

ക്ലിനിക്കൽ സവിശേഷതകളാൽ എന്താണ് അർത്ഥമാക്കുന്നത്: രോഗിയുടെ പ്രായം, രോഗത്തിൻറെ ലക്ഷണങ്ങളും അടയാളങ്ങളും, മുൻകാല മെഡിക്കൽ ചരിത്രം, ചികിത്സയ്ക്കുള്ള പ്രതികരണം തുടങ്ങിയ പാരാമീറ്ററുകൾ ഞങ്ങൾ പഠിക്കുമെന്ന് ക്ലിനിക്കൽ സവിശേഷതകൾ അർത്ഥമാക്കുന്നു.

എന്താണ് കാർഡിയാക് മാഗ്നെറ്റിക് റെസൊണൻസ്: ഹൃദയസ്തംഭനം പോലുള്ള വിവിധ രോഗങ്ങളിൽ ഹൃദയത്തിന്റെ അവസ്ഥ നന്നായി മനസിലാക്കാൻ അടുത്തിടെ ഉപയോഗിക്കുന്ന ഒരു നൂതന അന്വേഷണമാണ് കാർഡിയാക് മാഗ്നെറ്റിക് റെസൊണൻസ്. ഇത് ഒരു എം ആർ ഐ മെഷീൻ ഉപയോഗിച്ചാണ് നടത്തുന്നത്, കൂടാതെ എക്സ്-റേ അല്ലെങ്കിൽ സിടി സ്കാൻ മെഷീൻ പോലുള്ള ചിത്രങ്ങളോ ചിത്രങ്ങളോ നിർമ്മിക്കുന്നു. സി എം ആറിൽ കുത്തിവയ്പ്പുകളോ മറ്റ് മരുന്നുകളോ നൽകുന്നില്ല, മാത്രമല്ല രോഗിക്ക് വേദനയുമില്ല. എന്നിരുന്നാലും, അന്വേഷണത്തിന് വളരെയധികം സമയമെടുക്കുന്നു (ഏകദേശം 60 - 70 മിനിറ്റ്) രോഗി മെഷീനിനുള്ളിൽ നിശബ്ദമായി കിടക്കേണ്ടതുണ്ട്.

ഇതിൽ ഏതെങ്കിലും ഇടപെടൽ നടപടിക്രമങ്ങൾ ഉൾപ്പെടുന്നുണ്ടോ? ഇല്ല. ഇതിനകം സൂചിപ്പിച്ചതുപോലെ, മരുന്നുകൾ, പ്രവർത്തനം അല്ലെങ്കിൽ കുത്തിവയ്പ്പുകൾ എന്നിവയുടെ രൂപത്തിൽ സി എം ആറിൽ ഒരു ഇടപെടലും ഉൾപ്പെടില്ല

നിങ്ങൾ പങ്കെടുക്കുകയാണെങ്കിൽ നിങ്ങൾ എന്തുചെയ്യണം? ഈ പഠനത്തിൽ പങ്കെടുക്കുന്നതിൽ അധിക ചികിത്സാ നടപടിക്രമങ്ങളോ ആശുപത്രിയിൽ പ്രവേശിക്കുന്ന കാലാവധിയോ ഉൾപ്പെടില്ല. സംരക്ഷിത എജക്ഷൻ ഭിന്നസംഖ്യ ഉപയോഗിച്ച് ഹൃദയസ്തംഭനത്തിന് നിങ്ങളുടെ ഡോക്ടർ സി എം ആർ നിർദ്ദേശിക്കുകയാണെങ്കിൽ മാത്രമേ ഈ പഠനത്തിൽ പങ്കെടുക്കാൻ നിങ്ങളോട് അഭ്യർത്ഥിക്കുകയുള്ളൂ. സി എം ആറിന്റെ വില ഉൾപ്പെടെ ചികിത്സയുടെ സാധാരണ ചെലവ് നിങ്ങൾ വഹിക്കേണ്ടതുണ്ട്. അധികച്ചെലവുകളൊന്നും ഈടാക്കില്ല, കൂടാതെ അധിക മരുന്നുകളൊന്നും നിങ്ങൾക്ക് നൽകില്ല.

ഈ പഠനം ആരംഭിച്ചതിന് ശേഷം നിങ്ങൾക്ക് അതിൽ നിന്ന് പിന്മാറാൻ കഴിയുമോ? അതെ. ഈ പഠനത്തിലെ നിങ്ങളുടെ പങ്കാളിത്തം പൂർണ്ണമായും

സ്വമേധയാ ഉള്ളതാണ്, പഠനത്തിൽ നിന്ന് പങ്കെടുക്കാനുള്ള അനുമതി പിൻവലിക്കാൻ നിങ്ങൾക്ക് സ്വാതന്ത്ര്യമുണ്ട്. നിങ്ങൾ അങ്ങനെ ചെയ്യുകയാണെങ്കിൽ, കാർഡിയാക് മാഗ്നെറ്റിക് റെസൊണൻസ് പഠനത്തിനുള്ള നിങ്ങളുടെ യോഗ്യത ഉൾപ്പെടെ ഈ ആശുപത്രിയിലെ നിങ്ങളുടെ സാധാരണ ചികിത്സയെ ഇത് ബാധിക്കില്ല.

ഈ പഠനവുമായി ബന്ധപ്പെട്ട് എന്തെങ്കിലും അപകടസാധ്യതയുണ്ടോ എന്ന്? ഇത് ഒരു നിരീക്ഷണ പഠനമായതിനാൽ രോഗിക്ക് വ്യക്തിഗത അപകടസാധ്യതയോ നേട്ടമോ ഇല്ല.

നിങ്ങളുടെ സ്വകാര്യ വിശദാംശങ്ങൾ രഹസ്യമായി സൂക്ഷിക്കുമോ? ഈ പഠന ഫലങ്ങൾ ഒരു മെഡിക്കൽ ജേണലിൽ പ്രസിദ്ധീകരിക്കും, പക്ഷേ ഫലങ്ങളുടെ പ്രസിദ്ധീകരണത്തിലോ അവതരണത്തിലോ നിങ്ങളെ പേര് ഉപയോഗിച്ച് തിരിച്ചറിയാൻ കഴിയില്ല. എന്നിരുന്നാലും, പഠനത്തിൽ പങ്കെടുക്കാൻ നിങ്ങൾ തീരുമാനിക്കുകയാണെങ്കിൽ നിങ്ങളുടെ അധിക അനുമതിയില്ലാതെ പഠനവുമായി ബന്ധപ്പെട്ട ആളുകൾ നിങ്ങളുടെ മെഡിക്കൽ കുറിപ്പുകൾ അവലോകനം ചെയ്തേക്കാം.

ഏത് സമയത്തും നിങ്ങൾക്ക് എന്തെങ്കിലും പ്രശ്നങ്ങൾ അനുഭവപ്പെടുകയോ അല്ലെങ്കിൽ നിങ്ങൾക്ക് കൂടുതൽ ചോദ്യങ്ങൾ ഉണ്ടെങ്കിലോ, നിങ്ങൾക്ക് ബന്ധപ്പെടാൻ സ്വാതന്ത്ര്യമുണ്ട് :

1.**ഡോ. സുദിപ്ത മൊണ്ടാൽ**, പ്രിൻസിപ്പൽ ഇൻവെസ്റ്റിഗേറ്റർ (sudiptamondalnrs@gmail.com, 7686906481) അല്ലെങ്കിൽ

2.**ഡോ. ശ്രീനിവാസ് ജി**, അംഗം സെക്രട്ടറി, ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്കൽ കമ്മിറ്റി, എസ് സി ടി എം ടി, തിരുവനന്തപുരം

Annexure

Clinical and Cardiac Magnetic Resonance (CMR) features in Heart Failure with preserved ejection fraction (HFpEF)

Principal Investigator: Dr Sudipta Mondal, DM Cardiology Resident, SCTIMST, Trivandrum

Participant consent form

Please tick as appropriate

I confirm that **I have read and understood the information sheet** for study participants for this study on …….. (date) and have had the opportunity to ask questions which have been answered fully and to my satisfaction	**Yes / No**
I understand that **my participation is voluntary and I am free to withdraw at any time**, without giving any reason, without my medical care or legal rights being affected.	**Yes / No**
I understand that sections of any of my medical notes may be looked at by responsible individuals from **Sree Chitra Institute for Medical Sciences and Technology**, where it is relevant to my taking part in this research. I give permission for these individuals to access my records that are relevant to this research.	**Yes / No**
I agree to take part in the above study.	**Yes / No**

Name of the participant **Signature** **Date**

In case the patient is illiterate, representative / next of kin shall sign on his / her behalf:

Name **Relationship with the patient** **Signature** **Date**

Name of the Principal Investigator **Signature** **Date**

Annexure

क्लिनिकल और कार्डिएक मैग्नेटिक रेजोनेंस (सीएमआर) हार्ट फेल्योर में संरक्षित इजेक्शन फ्रैक्शन के साथ विशेषताएं

प्रधान अन्वेषक: डॉ सुदीप्त मंडल, डीएम कार्डियोलॉजी रेजिडेंट, एससीटीआईएमएसटी, त्रिवेंद्रम

प्रतिभागी सहमति प्रपत्र

कृपया उपयुक्त के रूप में टिक करें

मैं पुष्टि करता/करती हूं कि मैंने ..... को इस अध्ययन के लिए अध्ययन प्रतिभागियों के लिए सूचना पत्र पढ़ और समझ लिया है। (तारीख) और मुझे ऐसे प्रश्न पूछने का अवसर मिला है जिनका पूरी तरह से और मेरी संतुष्टि के लिए उत्तर दिया गया है	हाँ / नही
मैं समझता/समझती हूं कि मेरी भागीदारी स्वैच्छिक है और मैं बिना कोई कारण बताए, मेरी चिकित्सा देखभाल या कानूनी अधिकारों को प्रभावित किए बिना किसी भी समय वापस लेने के लिए स्वतंत्र हूं।	हाँ / नही
मैं समझता/समझती हूं कि मेरे किसी भी मेडिकल नोट के अनुभागों को श्री चित्रा इंस्टीट्यूट फॉर मेडिकल साइंसेज एंड टेक्नोलॉजी के जिम्मेदार व्यक्तियों द्वारा देखा जा सकता है, जहां यह इस शोध में मेरे भाग लेने के लिए प्रासंगिक है। मैं इन व्यक्तियों को इस शोध के लिए प्रासंगिक अपने रिकॉर्ड तक पहुंचने की अनुमति देता हूं।	हाँ / नही
मैं उपरोक्त अध्ययन में भाग लेने के लिए सहमत हूं।	हाँ / नही

प्रतिभागी का नाम हस्ताक्षर दिनांक

यदि रोगी निरक्षर है, तो उसकी ओर से प्रतिनिधि/रिश्तेदारों को हस्ताक्षर करना होगा:

नाम रोगी के साथ संबंध हस्ताक्षर दिनांक

डॉ सुदीप्त मंडल (प्रधान अन्वेषक) हस्ताक्षर दिनांक

Annexure

സംരക്ഷിത എജക്ഷൻ ഫ്രാക്ഷൻ (എച്ച്എഫ് പിഇഎഫ്) ഉള്ള ഹാർട്ട് പരാജയത്തിലെ ക്ലിനിക്കൽ, കാർഡിയാക് മാഗ്നറ്റിക് റെസൊണൻസ് (സിഎംആർ) സവിശേഷതകൾ

പ്രിൻസിപ്പൽ ഇൻവസ്റ്റിഗേറ്റർ: ഡാ. സുദിപ്ത മണ്ടാൽ, ഡിഎം കാർഡിയൊളജി റെസിഡന്റ്, എസ് സിടിഎംഎസ്ടി, തിരുവനന്തപുരം

പങ്കെടുക്കുന്നവരുടെ സമ്മതപത്രം

ഉചിതമായത് ടിക്ക് ചെയ്യുക

ഈ പഠനത്തിനായി പഠനത്തിൽ പങ്കെടുക്കുന്നവർക്കുള്ള വിവര ഷീറ്റ് ഞാൻ വായിക്കുകയും മനസ്സിലാക്കുകയും ചെയ്തുവെന്ന് ഞാൻ സ്ഥിരീകരിക്കുന്നു ..... (തീയതി) കൂടാതെ എനിക്ക് പൂർണ്ണമായി ഉത്തരും ലഭിച്ച ചൊദ്യങ്ങൾ ചൊദിക്കാനുള്ള അവസരും ലഭിച്ചു. **അതെ / ഇല്ല**

എൻറെ പങ്കാളിത്തം സ്വമധയാ ഉള്ളതാണ് എന്നും

വൈദ്യസഹായമായും നിയമപരമായ അവകാശങ്ങളൊ ബാധിക്കാതെ ഏത് സമയത്തും പിൻവലിക്കാൻ എനിക്ക് സ്വാതന്ത്ര്യം ഉണ്ടെന് ഞാൻ മനസ്സിലാക്കുന്നു. **അതെ / ഇല്ല**

എന്റെ ഏതെങ്കിലും മെഡിക്കൽ കുറിപ്പുകളുടെ ഭാഗങ്ങൾ ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് & ടെക്നോളജിയിൽ നിന്നുള്ള ഉത്തരവാദിത്തമുള്ള വ്യക്തികൾക്ക് ഉണ്ടെന് ഞാൻ മനസ്സിലാക്കുന്നു. ഈ ഗവേഷണത്തിന് പ്രസക്തമായ എന്റെ രേഖകൾ ആകസസ് ചെയ്യാൻ ഞാൻ അനുമതി നൽകുന്നു. **അതെ / ഇല്ല**

മുകളിലുള്ള പഠനത്തിൽ പങ്കെടുക്കാൻ ഞാൻ സമ്മതിക്കുന്നു

അതെ / ഇല്ല

പങ്കെടുക്കുന്നയാളുടെ പേര് ഒപ്പ് തീയതി

രോഗി നിരക്ഷരനാണെങ്കിൽ, പ്രതിനിധി / അടുത്ത ബന്ധു അവന് / അവൾക്ക് വേണ്ടി ഒപ്പിടും :

പേര്

രോഗിയുമായുള്ള ബന്ധം ഒപ്പ്. തീയതി

പ്രിൻസിപ്പൽ ഇൻവെസ്റ്റിഗേറ്റർ. ഒപ്പ്. തീയതി

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
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Institutional Ethics Committee

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

SCT/IEC/1881/MAY/2022

03.09.2022

Dr. Sudipta Mondal
Senior Resident
Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Sudipta Mondal,

The Institutional Ethics Committee held on 13th May, 2022, reviewed and discussed your application to conduct the study titled "**CLINICAL AND CARDIAC MAGNETIC RESONANCE (CMR) FEATURES IN HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFPEF)**" (IEC/1881).

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

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

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the Chairperson, IEC, SCTIMST*
2. *Checklist Form*
3. *Declaration form*
4. *IEC Application Form*
5. *Responses / Amendments made based on the Reviewer's comments*
6. *Project Proposal*
7. *CV of PI and Co-PI s*
8. *Proforma*
9. *Participant Consent Form in English, Hindi and Malayalam*
10. *Information Sheet for study participants English, Hindi and Malayalam*
11. *SRC Recommendation letter*

Revised submission

1. *Covering letter addressed to the Member Secretary, IEC, SCTIMST*
2. *Covering letter addressed to the Chairperson, IEC, SCTIMST*
3. *Checklist Form*
4. *Declaration form*
5. *IEC Application Form*
6. *Responses / Amendments made based on the Reviewer's comments*
7. *Project Proposal*
8. *CV of PI and Co-PI s*
9. *Proforma*
10. *Participant Consent Form in English, Hindi and Malayalam*
11. *Information Sheet for study participants English, Hindi and Malayalam*

IEC Decision

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

Remarks:

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

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

Sincerely,

Dr. G. Srinivas
Member Secretary, IEC

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST, THIRUVANANTHAPURAM

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

Master Chart **Sheet A**

Sl No	Age	Sex	Ht (cm)	Wt (kg)	BMI	BSA	PRO BNP	HB	CR	TSH	HTN	DM
	49	F	152	65	28.1	1.62	216	12.3	1	2.5	1	0
	62	F	146	78	36.6	1.70	1170	12.6	1.01	2.9	1	1
	62	F	148	67	30.6	1.61	152	12.8	0.9	3.4	1	1
	63	F	155	60	25.0	1.59	325	13	0.86	4.5	1	0
	47	M	166	85	30.8	1.93	404	15.6	1.33	1.7	0	0
	60	F	144	41	19.8	1.28	168	13	0.9	4.7	1	0
	72	F	153	80	34.2	1.77	638	12	1	4	1	1
	64	F	155	60	25.0	1.59	350	13.1	0.9	4.5	1	0
	48	M	166	85	30.8	1.93	402	16	1.3	1.7	0	0
	74	F	153	80	34.2	1.77	713	11.9	1.1	4	1	1
	50	F	152	65	28.1	1.62	201	12.9	1	2.5	1	0
	63	F	146	78	36.6	1.70	1300	12.6	1.1	2.9	1	1
	63	F	148	67	30.6	1.61	156	12.9	0.9	3.4	1	1
	61	F	144	41	19.8	1.28	167	12.8	0.9	4.7	1	0
	59	F	150	87	38.7	1.81	682	16.9	0.44	2.3	1	1
	74	M	164	84	31.2	1.91	5500	13.9	1.09	2.4	1	0
	65	F	148	57	26.0	1.50	177	14.5	0.9	1.2	1	0
	69	F	154	60	25.3	1.58	1640	12.3	1.5	2.9	1	0
	68	F	144	65	31.3	1.55	1400	13	1.5	3	1	1
	55	F	146	65	30.5	1.57	29100	10.4	0.7	1.8	1	0
	66	F	143	58	28.4	1.47	1760	12.9	1	3.3	1	1
	74	F	143	52	25.4	1.41	4180	11.1	0.8	3	0	0
	64	F	148	57	26.0	1.50	180	14	0.9	1.2	1	0
	60	F	150	87	38.7	1.81	700	17	0.6	2.3	1	1
	73	F	143	52	25.4	1.41	5001	11.1	0.8	3	0	0
	73	M	164	84	31.2	1.91	5600	14.1	1.09	2.4	1	0
	69	F	144	65	31.3	1.55	1507	12	1.5	3	1	1
	65	F	143	58	28.4	1.47	1670	12.9	1	3.3	1	1
	68	F	153	60	25.6	1.57	1709	12.3	1.46	2.9	1	0
	56	F	146	65	30.5	1.57	28000	11	0.7	1.8	1	0

HYPO T4	COPD	CAD	DYSLIPID	OBESITY	OSA	F/H/O CAD	HX COVID	INDEX EVENT	TYPE	F/U duration	F/U EVENT
0	1	0	0	2	0	0	1	0	OP	8	0
0	1	0	0	1	0	0	0	0	OP	8	0
0	0	0	1	1	0	0	0	0	OP	24	0
0	0	0	1	0	0	0	0	0	OP	18	0
0	0	0	0	1	0	0	0	0	OP	42	0
0	0	1	1	0	0	1	0	0	OP	44	0
1	0	0	0	1	0	0	0	0	OP	52	0
0	0	0	1	0	0	0	0	0	OP	18	0
0	0	0	0	1	0	0	0	0	OP	42	0
1	0	0	0	1	0	0	0	0	OP	52	0
0	1	0	0	2	0	0	1	0	OP	8	0
0	1	0	0	1	0	0	0	0	OP	8	0
0	0	0	1	1	0	0	0	0	OP	24	0
0	0	1	1	0	0	1	0	0	OP	44	0
0	0	1	1	1	1	0	1	1	HF	11	0
0	1	0	0	1	1	0	0	1	HF	23	0
0	0	0	1	2	0	0	0	1	HF	48	0
0	0	0	1	2	0	0	0	1	AF	18	0
0	0	0	1	1	0	0	0	1	HF	22	1
0	0	0	0	1	0	0	0	1	HF	11	0
0	0	0	0	2	0	0	0	0	OP	9	1
0	1	1	0	2	0	0	0	1	AF HF	48	1
0	0	0	1	2	0	0	0	1	HF	48	0
0	0	1	1	1	1	0	1	1	HF	12	0
0	1	1	0	2	0	0	0	1	AF HF	48	1
0	1	0	0	1	1	0	0	1	HF	23	0
0	0	0	1	1	0	0	0	1	HF	22	1
0	0	0	0	2	0	0	0	0	OP	9	1
0	0	0	1	2	0	0	0	1	AF	18	0
0	0	0	0	1	0	0	0	1	HF	11	0

ANY EVENT	SOB	FC	PND	COUGH	EXPECT	ANAS	OLIGURIA	ANGINA	PALPIT	SYNC	SGLT2I
0	1	2	0	0	0	0	0	0	0	0	0
0	1	3	0	1	0	0	0	1	0	0	1
0	1	2	0	0	0	0	0	1	0	0	0
0	1	2	0	0	0	0	0	0	1	0	0
0	1	2	0	0	0	0	0	0	1	0	0
0	1	2	0	0	0	0	0	1	0	0	0
0	1	2	0	0	0	0	0	0	0	0	0
0	1	2	0	0	0	0	0	0	1	0	0
0	1	2	0	0	0	0	0	0	1	0	0
0	1	2	0	0	0	0	0	0	0	0	0
0	1	2	0	0	0	0	0	0	0	0	0
0	1	3	0	1	0	0	0	1	0	0	1
0	1	2	0	0	0	0	0	1	0	0	0
0	1	2	0	0	0	0	0	1	0	0	0
1	1	4	1	1	0	0	0	0	0	0	1
1	1	2	0	0	0	0	0	0	1	0	0
1	1	3	0	1	0	0	0	0	0	0	0
1	1	2	0	0	0	0	0	0	1	0	0
1	1	3	0	1	0	0	0	0	0	0	0
1	1	4	1	0	0	0	0	0	1	0	1
1	1	2	0	0	0	0	0	0	0	0	1
1	1	4	1	1	0	0	0	0	1	0	0
1	1	3	0	1	0	0	0	0	0	0	0
1	1	4	1	1	0	0	0	0	0	0	1
1	1	4	1	1	0	0	0	0	1	0	0
1	1	2	0	0	0	0	0	0	1	0	0
1	1	3	0	1	0	0	0	0	0	0	0
1	1	2	0	0	0	0	0	0	0	0	1
1	1	2	0	0	0	0	0	0	1	0	0
1	1	4	1	0	0	1	0	0	1	0	1

Loop Diuretic	Frusemide equivalent dose /day	MRA	Dose/day	PR	PULSE CHAR	SBP	DBP	HTN @VISIT	RR	Sat RA %	JVP	RALES
1	20	1	25	75	0	150	80	1	15	96	0	1
1	10	1	12.5	64	0	218	103	1	14	98	0	0
1	20	0	0	81	0	188	93	1	13	99	0	0
0	0	1	25	59	0	150	84	1	13	99	0	0
1	40	1	12.5	64	0	116	80	0	12	99	0	0
0	0	0	0	77	0	147	82	1	12	99	0	0
1	10	0	0	82	0	144	70	1	13	100	0	0
0	0	1	25	60	0	148	86	1	13	99	0	0
1	40	1	12.5	65	0	114	80	0	12	99	0	0
1	10	0	0	81	0	146	72	1	13	100	0	0
1	20	1	25	76	0	154	80	1	15	96	0	1
1	10	1	12.5	65	0	216	100	1	14	98	0	0
1	20	0	0	87	0	188	94	1	13	99	0	0
0	0	0	0	70	0	148	84	1	12	99	0	0
1	40	0	0	70	0	151	78	1	30	84	1	1
1	20	0	0	77	0	120	66	0	14	99	0	0
1	40	1	25	55	0	144	68	1	14	98	0	0
1	40	1	25	90	0	121	84	0	13	99	0	0
1	60	0	0	78	0	125	69	0	18	98	0	0
1	80	1	25	112	1	170	110	1	29	88	1	1
0	0	0	0	76	0	243	74	1	17	98	0	0
1	20	1	50	140	1	110	88	0	24	94	1	1
1	40	1	25	54	0	146	70	1	14	98	0	0
1	40	0	0	71	0	154	78	1	30	82	1	1
1	20	1	50	130	0	114	84	0	24	94	1	1
1	20	0	0	78	0	124	66	0	14	99	0	0
1	60	0	0	77	0	126	70	0	18	98	0	0
0	0	0	0	76	0	220	74	1	17	98	0	0
1	40	1	25	91	0	122	84	0	13	99	0	0
1	80	1	25	114	1	172	110	1	29	88	1	1

S1	LOUD P2	GALLOP	MURMUR	OUTPUT	PED EDEMA	SR	LAE	PR	QRS AXIS	QRSD	QRS Morphol	QTC
N	1	0	0	0	0	1	0	140	36	70	N	419
N	0	0	0	0	0	1	1	150	-10	150	LBBB	415
N	0	0	0	0	0	1	0	140	26	80	N	396
N	0	0	0	0	1	1	1	160	22	80	N	409
N	0	0	1	0	0	0	NA	NA	0	70	N	400
N	0	0	0	0	0	1	0	120	70	70	N	438
N	0	0	0	0	0	1	0	155	48	70	N	418
N	0	0	0	0	1	1	1	170	25	80	N	409
N	0	0	1	0	0	0	NA	NA	0	70	N	400
N	0	0	0	0	0	1	0	150	48	70	N	418
N	1	0	0	0	0	1	0	140	36	70	N	419
N	0	0	0	0	0	1	1	160	-10	160	LBBB	415
N	0	0	0	0	0	1	0	140	26	80	N	396
N	0	0	0	0	0	1	0	130	70	70	N	438
N	1	1	1	0	1	1	1	170	30	70	N	378
N	0	0	0	0	1	1	0	140	51	70	N	418
N	0	0	0	0	0	1	0	200	-5	140	LBBB	415
N	1	0	0	0	0	0	NA	NA	36	70	N	354
N	0	0	0	0	1	1	1	200	21	70	N	425
N	1	1	1	1	1	1	0	140	70	65	N	403
N	0	0	0	0	0	1	0	150	70	96	N	405
N	1	1	0	0	0	0	NA	NA	-71	142	RBBB	370
N	0	0	0	0	0	1	0	200	-5	146	LBBB	415
N	1	1	1	0	1	1	1	170	35	70	N	378
N	1	1	0	0	0	0	NA	NA	-70	142	RBBB	370
N	0	0	0	0	1	1	0	160	51	70	N	418
N	0	0	0	0	1	1	1	200	21	70	N	425
N	0	0	0	0	0	1	0	160	70	96	N	405
N	1	0	0	0	0	0	NA	NA	36	70	N	354
N	1	1	1	1	1	1	0	140	70	65	N	403

LVH	ST T CHANGES	CE	CTR %	LAE	Carinal angle	PVH GRADE	PAH	LUN FIELD ABN	LVIDD	LVIDS	IVS D	IVS S
1	0	1	55	1	90	1	1	0	48	32	12	13
0	1	1	60	1	88	1	1	0	47	31	12	13
0	1	0	48	0	74	1	0	0	43	29	11	16
0	0	1	51	0	75	0	0	0	48	25	11	13
0	0	0	50	0	72	1	0	0	49	32	10	14
0	1	1	51	0	71	1	0	0	41	22	13	14
0	1	0	50	0	69	1	0	0	50	31	10	11
0	0	1	52	0	75	0	0	0	48	25	11	13
0	0	0	50	0	73	1	0	0	49	32	10	14
0	1	0	50	0	69	1	0	0	50	31	10	12
1	0	1	56	1	90	1	1	0	48	32	12	14
0	1	1	61	1	88	1	1	0	47	31	12	13
0	1	0	49	0	73	1	0	0	43	29	11	16
0	1	1	51	0	72	1	0	0	41	22	13	14
1	1	1	62	1	73	3	1	1	44	24	14	16
0	0	1	57	1	81	1	1	0	44	29	11	12
0	1	0	49	0	70	1	1	0	44	27	10	15
0	0	1	62	1	85	1	1	0	48	27	10	13
0	1	1	66	1	84	2	1	0	37	27	18	19
0	1	1	59	1	98	3	1	1	47	30	10	11
0	0	1	64	1	91	2	1	0	43	27	14	15
0	0	1	65	1	93	3	1	0	50	33	14	16
0	1	0	48	0	71	1	1	0	44	27	10	14
1	1	1	63	1	72	2	1	1	44	24	14	16
0	0	1	66	1	91	3	1	0	50	33	14	16
0	0	1	58	1	82	1	1	0	44	29	11	13
0	1	1	65	1	83	2	1	0	37	27	18	20
0	0	1	63	1	92	2	1	0	43	27	14	15
0	0	1	63	1	85	1	1	0	48	27	10	13
0	1	1	59	1	97	3	1	1	47	30	10	12

PWD	PWS	LV mass	LV mass in	LV mass Th	LVMI Th	RWT	HYPERTROPHY	ECHO LVH	RVID	EF	FS	LA PLAX
11	16	206.4	127.6	184	114	0.46	CH	1	33	56	33	44
12	13	212.0	124.9	188	111	0.51	CH	1	25	61	34	36
11	16	162.9	101.4	151	94	0.51	CH	1	22	61	33	38
9	12	170.2	107.4	157	99	0.38	EH	1	20	69	48	40
10	13	176.0	91.1	162	84	0.41	N	0	22	65	35	50
11	12	171.7	134.4	158	123	0.54	CH	1	21	75	46	40
10	11	182.0	102.5	167	94	0.40	EH	1	21	67	38	40
9	12	170.2	107.4	157	99	0.38	EH	0	20	69	48	42
10	13	176.0	91.1	162	84	0.41	N	0	22	65	35	51
10	11	182.0	102.5	167	94	0.40	EH	1	21	67	38	40
11	16	206.4	127.6	184	114	0.46	CH	1	33	56	33	44
12	13	212.0	124.9	188	111	0.51	CH	1	25	61	34	35
11	16	162.9	101.4	151	94	0.51	CH	1	22	61	33	39
11	12	171.7	134.4	158	123	0.54	CH	1	21	75	46	40
13	15	227.5	125.5	199	110	0.59	CH	1	29	77	45	38
11	12	168.9	88.7	155	82	0.50	CR	0	21	61	34	43
9	12	137.8	91.9	131	87	0.41	N	0	26	70	39	42
10	13	170.2	107.9	157	100	0.42	EH	1	23	74	44	42
15	17	243.8	156.8	212	136	0.81	CH	1	23	53	27	46
8	11	142.7	90.9	135	86	0.34	N	0	24	64	36	30
14	16	232.2	157.6	203	137	0.65	CH	1	21	69	37	40
12	14	261.8	186.1	225	160	0.48	CH	1	22	63	34	46
9	12	137.8	91.9	131	87	0.41	N	0	26	70	39	43
13	15	227.5	125.5	199	110	0.59	CH	1	29	77	45	40
12	14	261.8	186.1	225	160	0.48	CH	1	22	63	34	46
11	12	168.9	88.7	155	82	0.50	CR	0	21	61	34	42
15	17	243.8	156.8	212	136	0.81	CH	1	23	53	27	46
14	16	232.2	157.6	203	137	0.65	CH	1	21	69	37	42
10	13	170.2	108.4	157	100	0.42	EH	1	23	74	44	43
8	11	142.7	90.9	135	86	0.34	N	0	24	64	36	30

PWD	PWS	LV mass	LV mass in	LV mass Th	LVMI Th	RWT	HYPERTROPHY	ECHO LVH	RVID	EF	FS	LA PLAX
11	16	206.4	127.6	184	114	0.46	CH	1	33	56	33	44
12	13	212.0	124.9	188	111	0.51	CH	1	25	61	34	36
11	16	162.9	101.4	151	94	0.51	CH	1	22	61	33	38
9	12	170.2	107.4	157	99	0.38	EH	1	20	69	48	40
10	13	176.0	91.1	162	84	0.41	N	0	22	65	35	50
11	12	171.7	134.4	158	123	0.54	CH	1	21	75	46	40
10	11	182.0	102.5	167	94	0.40	EH	1	21	67	38	40
9	12	170.2	107.4	157	99	0.38	EH	0	20	69	48	42
10	13	176.0	91.1	162	84	0.41	N	0	22	65	35	51
10	11	182.0	102.5	167	94	0.40	EH	1	21	67	38	40
11	16	206.4	127.6	184	114	0.46	CH	1	33	56	33	44
12	13	212.0	124.9	188	111	0.51	CH	1	25	61	34	35
11	16	162.9	101.4	151	94	0.51	CH	1	22	61	33	39
11	12	171.7	134.4	158	123	0.54	CH	1	21	75	46	40
13	15	227.5	125.5	199	110	0.59	CH	1	29	77	45	38
11	12	168.9	88.7	155	82	0.50	CR	0	21	61	34	43
9	12	137.8	91.9	131	87	0.41	N	0	26	70	39	42
10	13	170.2	107.9	157	100	0.42	EH	1	23	74	44	42
15	17	243.8	156.8	212	136	0.81	CH	1	23	53	27	46
8	11	142.7	90.9	135	86	0.34	N	0	24	64	36	30
14	16	232.2	157.6	203	137	0.65	CH	1	21	69	37	40
12	14	261.8	186.1	225	160	0.48	CH	1	22	63	34	46
9	12	137.8	91.9	131	87	0.41	N	0	26	70	39	43
13	15	227.5	125.5	199	110	0.59	CH	1	29	77	45	40
12	14	261.8	186.1	225	160	0.48	CH	1	22	63	34	46
11	12	168.9	88.7	155	82	0.50	CR	0	21	61	34	42
15	17	243.8	156.8	212	136	0.81	CH	1	23	53	27	46
14	16	232.2	157.6	203	137	0.65	CH	1	21	69	37	42
10	13	170.2	108.4	157	100	0.42	EH	1	23	74	44	43
8	11	142.7	90.9	135	86	0.34	N	0	24	64	36	30

LA A4C L	LA A4C W	LAV	LAVI	LAE	Ao	RWMA	MV E	MV A	EDT	L wave	LAT E'	LAT E/E'
49	37	41.7	25.8	0	30	N	1.1	0.87	145	0	8.5	12.9
47	34	30.1	17.7	0	27	N	1.4	0.6	162	1	6.3	22.2
54	40	42.9	26.7	0	30	N	1	1.3	166	0	9.9	10.1
53	49	54.3	34.3	1	28	N	1.2	0.9	129	1	9.6	12.5
70	50	91.5	47.4	1	31	N	1.2	NA	128	0	3.3	36.4
51	40	42.7	33.4	0	29	N	1	0.8	160	0	10	10.0
52	36	39.2	22.1	0	33	N	1.1	0.85	160	0	8.5	12.9
53	49	57.0	36.0	1	28	N	1.2	0.9	129	1	9.6	12.5
72	50	96.0	49.7	1	31	N	1.2	NA	128	0	3.3	36.4
52	36	39.2	22.1	0	33	N	1.1	0.85	160	0	8.5	12.9
49	37	41.7	25.8	0	30	N	1.1	0.87	145	0	8.5	12.9
48	35	30.8	18.1	0	27	N	1.4	0.6	162	1	6.3	22.2
53	41	44.3	27.6	0	30	N	1	1.3	166	0	9.9	10.1
51	40	42.7	33.4	0	29	N	1	0.8	160	0	10	10.0
51	40	40.5	22.4	0	31	N	0.6	0.7	180	0	6.5	9.2
57	40	51.3	26.9	0	33	N	0.8	1.1	160	0	7.7	10.4
53	43	50.1	33.4	0	22	N	1.7	1.3	230	1	9	18.9
67	49	72.1	45.7	1	29	N	1.6	NA	106	0	10	16.0
51	32	39.3	25.3	0	32	N	0.7	0.6	110	0	3.6	19.4
65	34	34.7	22.1	0	25	N	0.6	0.9	140	0	9	6.7
57	48	57.2	38.8	1	24	N	1.2	0.63	193	0	7	17.1
58	45	62.8	44.6	1	37	Y	0.9	1.1	135	0	4.5	20.0
53	43	51.3	34.2	1	22	N	1.7	1.3	230	1	9	18.9
51	40	42.7	23.5	0	31	N	0.6	0.7	180	0	6.5	9.2
58	45	62.8	44.6	1	37	Y	0.9	1.1	135	0	4.5	20.0
57	40	50.1	26.3	0	33	N	0.8	1.1	160	0	7.7	10.4
52	33	41.3	26.6	0	32	N	0.7	0.6	110	0	3.6	19.4
57	48	60.1	40.8	1	24	N	1.2	0.63	193	0	7	17.1
68	49	74.9	47.7	1	29	N	1.6	NA	106	0	10	16.0
65	34	34.7	22.1	0	25	N	0.6	0.9	140	0	9	6.7

MED E'	MED E/E'	AVG E/E'	LAT A'	MED A'	TR GRADE	TR GARDIENT	LVDD GARDE	TAPSE	AOV	PV	MR	AR
5.9	18.6	15.8	9.8	10	2	38	2	21	1.2	1.4	2	0
5.2	26.9	24.6	5.3	6.1	2	36	2	19	1	1	2	1
7.6	13.2	11.6	6.9	12.7	1	34	1	19	1.3	0.9	1	0
5.3	22.6	17.6	10	8.9	2	32	2	19	1.1	0.9	2	0
3	40.0	38.2	NA	NA	3	35	3	22	1.1	1	3	0
6	16.7	13.3	7	5	1	27	1	18	1	1	2	0
6.7	16.4	14.7	8.2	7.2	2	37	2	21	1.8	1.1	0	0
5.3	22.6	17.6	10	8.9	2	34	2	19	1.1	0.9	2	0
3	40.0	38.2	NA	NA	3	38	3	22	1.1	1	3	0
6.7	16.4	14.7	8.2	7.2	2	37	2	21	1.8	1.1	0	0
5.9	18.6	15.8	9.8	10	2	38	2	21	1.2	1.4	2	0
5.2	26.9	24.6	5.3	6.1	2	36	2	19	1	1	2	1
7.6	13.2	11.6	6.9	12.7	1	33	1	19	1.3	0.9	1	0
6	16.7	13.3	7	5	1	27	1	18	1	1	2	0
5.9	10.2	9.7	9.5	7.5	2	33	1	19	1.3	0.9	1	0
5	16.0	13.2	10	10	2	41	1	21	1.6	1.4	1	0
7	24.3	21.6	13	8.9	2	53	2	21	1.2	1	3	0
6.9	23.2	19.6	NA	NA	2	32	3	18	1.4	0.9	2	0
4.4	15.9	17.7	2.6	2.4	2	34	2	17	1.1	0.9	2	0
7	8.6	7.6	15	13	2	17	1	24	1.2	1.1	2	0
7	17.1	17.1	11	11	0	NA	2	21	1.6	0.9	2	0
4.3	20.9	20.5	7.6	8.4	2	35	2	24	2	1	2	1
7	24.3	21.6	13	8.9	2	54	2	21	1.2	1	3	0
5.9	10.2	9.7	9.5	7.5	2	35	1	19	1.3	0.9	1	0
4.3	20.9	20.5	7.6	8.4	2	33	2	24	2	1	2	1
5	16.0	13.2	10	10	2	42	1	21	1.6	1.4	1	0
4.4	15.9	17.7	2.6	2.4	2	33	2	17	1.1	0.9	2	0
7	17.1	17.1	11	11	0	NA	2	21	1.6	0.9	2	0
6.9	23.2	19.6	NA	NA	2	32	3	18	1.4	0.9	2	0
7	8.6	7.6	15	13	2	18	1	24	1.2	1.1	2	0

AS	PE	GLS ABN	BAS	BA	BAL	BIS	BI	BIL	MAS	MA	MAL	MIS
0	0	1	15	17	17	15	17	16	15	16	14	16
0	0	1	11	14	23	19	20	15	13	13	18	12
0	0	0	23	22	26	23	18	22	25	24	24	29
0	0	0	21	23	25	23	24	25	30	26	24	27
0	0	1	24	4	9	9	15	22	18	3	2	7
0	0	1	21	22	21	10	15	21	26	22	22	13
0	0	1	18	18	9	21	27	23	18	19	11	19
0	0	0	21	23	25	23	24	25	30	26	24	27
0	0	1	24	4	9	9	15	22	18	3	2	7
0	0	1	18	18	9	21	27	23	18	19	11	19
0	0	1	15	17	17	15	17	16	15	16	14	16
0	0	1	11	14	23	19	20	15	13	13	18	12
0	0	0	23	22	26	23	18	22	25	24	24	29
0	0	1	21	22	21	10	15	21	26	22	22	13
0	1	1	22	18	25	27	22	23	19	12	13	19
0	0	0	24	29	27	21	27	25	17	24	21	20
0	0	0	22	21	26	22	18	23	25	23	24	29
0	1	0	22	25	24	21	21	23	28	30	33	26
0	1	1	10	6	10	17	12	6	11	12	12	11
0	1	1	14	20	22	17	8	19	20	16	17	18
0	0	1	12	16	13	17	17	17	11	13	14	15
1	1	1	11	4	9	18	11	6	10	10	10	10
0	0	0	22	21	26	22	18	23	25	23	24	29
0	1	1	22	18	25	27	22	23	19	12	13	19
1	1	1	11	4	9	18	11	6	10	10	10	10
0	0	0	24	29	27	21	27	25	17	24	21	20
0	1	1	10	6	10	17	12	6	11	12	12	11
0	0	1	12	16	13	17	17	17	11	13	14	15
0	1	0	22	25	24	21	21	23	28	30	33	26
0	1	1	14	20	22	17	8	19	20	16	17	18

MI	MIL	AAS	AA	AAL	AIS	AI	AIL	CAD IN CAG	VESSEL	PA MEAN	PCWP	LVED
16	9	15	17	17	15	17	16	0				
11	15	17	17	20	12	11	15	0	CT			
17	19	25	29	24	29	28	17	0				
25	28	36	31	29	33	27	32	0				
17	16	20	12	4	10	23	14	0		26	12	10
14	20	19	20	20	16	17	17	1	RCA			
29	17	14	24	17	10	27	14	0	CT			
25	28	36	31	29	33	27	32	0				
17	16	20	12	4	10	23	14	0		26	12	10
29	17	14	24	17	10	27	14	0	CT			
16	9	15	17	17	15	17	16	0				
11	15	17	17	20	12	11	15	0	CT			
17	19	25	29	24	29	28	17	0				
14	20	19	20	20	16	17	17	1	RCA			
16	20	25	29	34	27	25	32	1	LAD	28	12	12
19	17	24	28	27	25	27	21	0				
18	18	24	30	23	30	27	16	0		26	15	12
27	34	35	30	46	41	41	47	0		24	24	19
15	7	11	19	17	10	12	15	0				
9	13	25	15	20	28	20	17	0		20	20	25
18	19	21	21	23	19	18	17	0	CT			
15	5	11	19	17	9	11	14	1	LCX			
18	18	24	30	23	30	27	16	0		26	15	12
16	20	25	29	34	27	25	32	1	LAD	28	12	12
15	5	11	19	17	9	11	14	1	LCX			
19	17	24	28	27	25	27	21	0				
15	7	11	19	17	10	12	15	0				
18	19	21	21	23	19	18	17	0	CT			
27	34	35	30	46	41	41	47	0		24	24	19
9	13	25	15	20	28	20	17	0		20	20	25

LA	LAV	LAVI	AO	LV ED Vol	LV ED vol index	LV ES vol	LV ES vol index	LV SV	LV SV INDEX	LV CO	LV CO INDEX	LV EF
48	42	26	31	98	61	29	17.9	69	42.7	5.2	3.2	70
40	37	22	33	71	42	26	15.3	45	26.5	3.1	1.8	63
38	49	30	30	121	75	46	28.6	75	46.7	6.9	4.3	62
44	55	34	28	115	73	30	18.9	82	51.7	4.2	2.6	71
53	81	42	22	119	62	44	22.8	75	38.8	5.6	2.9	63
42	43	34	30	93	73	25	19.6	68	53.2	4	3.1	73
40	45	25	29	58	33	25	14.1	33	18.6	2.9	1.6	57
46	57	36	32	109	69	43	27.1	66	41.6	5.3	3.3	61
43	53	28	28	112	58	30	15.5	82	42.4	4.2	2.2	73
47	60	34	25	126	71	52	29.3	74	41.7	5.7	3.2	59
58	87	54	31	123	76	57	35.3	66	40.8	5.1	3.2	54
44	41	24	29	90	53	32	18.9	58	34.2	4.1	2.4	64
46	59	37	30	110	68	40	24.9	70	43.6	5	3.1	64
41	61	48	37	102	80	44	34.4	58	45.4	3.4	2.7	57
38	39	21	33	128	71	28	15.4	100	55.2	6.7	3.7	78
42	50	26	27	113	59	30	15.7	83	43.6	4.3	2.3	73
53	81	54	24	120	80	44	29.3	76	50.7	5.5	3.7	63
49	44	28	31	99	63	32	20.3	67	42.5	5.1	3.2	68
43	67	43	35	105	68	41	26.4	64	41.2	2.6	1.7	61
58	92	58	30	125	80	50	31.8	75	47.8	5	3.2	60
42	43	29	32	82	56	24	16.3	58	39.4	3.3	2.2	71
39	40	29	32	124	88	30	21.3	94	66.8	5.7	4.1	76
45	58	38	31	110	73	42	28.0	68	45.3	5.2	3.5	62
39	50	28	29	120	66	45	24.8	75	41.4	6.5	3.6	63
46	60	43	30	115	82	35	24.9	80	56.9	4.8	3.4	70
43	54	29	28	110	58	35	18.4	82	43.0	4.6	2.4	75
41	41	26	29	94	60	26	16.7	68	43.7	4.1	2.6	72
45	40	27	30	94	64	34	23.1	60	40.7	4.3	2.9	64
40	47	30	29	62	39	24	15.3	38	24.2	3	1.9	61
48	64	41	27	128	82	48	31	80	51	5.9	3.8	63

RV ED VOL	RV ED VOL INDEX	RV ES VOL	RV ES VOL INDEX	RV STROKE VOL	RV STROKE VOL INDEX	RV CO	RV CO INDEX	RV EF	MV E	MV A
122	75.5	47	29.1	75	46.4	5.7	3.5	61	200	230
112	66.0	67	39.5	45	26.5	3.2	1.9	40	90	100
122	75.9	50	31.1	72	44.8	7	4.4	59	68	75
110	69.4	31	19.6	80	50.5	4.4	2.8	73	220	250
82	42.4	52	26.9	30	15.5	2.3	1.2	37	200	240
87	68.1	32	25.0	55	43.0	3.1	2.4	63	50	15
66	37.2	28	15.8	38	21.4	3.2	1.8	58	200	70
88	55.5	39	24.6	49	30.9	3.9	2.5	56	16	14
107	55.4	31	16.0	76	39.3	4.4	2.3	71	270	300
133	74.9	62	34.9	71	40.0	5.8	3.3	53	80	120
161	99.6	84	52.0	77	47.6	6	3.7	48	270	80
78	46.0	44	25.9	34	20.0	2.4	1.4	44		
90	56.0	38	23.7	52	32.4	4	2.5	58	40	60
82	64.2	38	29.7	44	34.4	2.6	2.0	54	100	110
123	67.9	52	28.7	71	39.2	4.9	2.7	58	55	65
105	55.1	33	17.3	72	37.8	4.5	2.4	69	250	300
83	55.3	51	34.0	32	21.3	2.4	1.6	39	190	250
121	76.7	48	30.4	73	46.3	5.5	3.5	60	170	180
90	57.9	39	25.1	51	32.8	2.9	1.9	57	90	110
145	92.3	65	41.4	80	50.9	5	3.2	55	250	90
121	82.1	69	46.8	52	35.3	3.3	2.2	43	80	100
120	85.3	48	34.1	72	51.2	5	3.6	60	65	75
90	60.0	40	26.7	50	33.3	3.8	2.5	56	20	18
121	66.8	52	28.7	69	38.1	6.9	3.8	57	66	75
96	68.2	43	30.6	53	37.7	4.1	2.9	55	123	60
109	57.2	38	19.9	80	42.0	4.2	2.2	73	120	250
88	56.6	33	21.2	55	35.4	3.2	2.1	63	55	20
82	55.6	46	31.2	36	24.4	2.6	1.8	44	150	160
63	40.1	25	15.9	38	24.2	3.1	2.0	60	190	75
135	86.0	63	40.1	72	45.8	5.9	3.8	53	150	180

LOCATION		PERFUSION	LOCATION PER	MR	%	BAS	BA	BAL	BIS	BI	BIL	B AVG
BAS, BIS	SE	0			8	1048	960	947	985	934	988	977
		0			11	1033	1116	1071	880	910	970	997
		0			33	1002	940	900	1040	1017	900	967
		0			11	1019	1027	1022	990	1036	1002	1016
		0			40	1032	1092	1023	1066	1100	992	1051
		0			8	1028	950	1018	950	1040	972	993
BAS, BIS	M	0			8	1008	1091	1157	993	984	1088	1054
BIS, BI, BIL	MM	0			10	1182	1246	1192	1080	1174	1300	1196
		0			19	1029	1006	1022	982	1036	993	1011
		0			20	1106	1045	1202	1123	1060	1248	1131
		0			15	1025	955	1028	955	1043	980	998
BAS, BIS	SE	1	BAS, BIS		20	1003	944	905	1043	1020	905	970
		0			8	1150	1196	1140	1050	1090	1245	1145
		0			7	1106	1100	1121	1096	1165	1153	1124
		0			7	976	1017	1003	1048	1019	966	1005
		0			18	1027	1005	1020	985	1035	990	1010
		0			33	1036	1090	1030	1068	1102	1001	1055
BAS, BIS	SE	0			9	1050	980	954	990	990	1000	994
		0			6	1114	1106	1123	1098	1165	1154	1127
		0			15	1002	945	1022	950	1044	990	992
		0			12	1043	1120	1076	890	920	990	1007
		0			5	972	1001	997	1043	1015	977	1001
BIS, BI, BIL	MM	0			8	1184	1250	1190	1082	1175	1301	1197
		0			23	1005	945	902	1050	1020	910	972
		0			6	1149	1196	1146	1050	1100	1245	1148
		0			9	1020	1027	1022	1011	1036	1012	1021
		0			5	1025	948	1010	954	1036	980	992
BAS, BIS	SE	1	BAS, BIS		20	1001	955	910	1045	1023	907	974
BAS, BIS	MM	0			9	1010	1094	1160	995	990	1090	1057
		0			11	1110	1051	1202	1140	1080	1249	1139

MAS	MA	MAL	MIS	MI	MIL	MID AVG T1	AAS	AA	AAL	AIS	AI	AIL
1082	1004	994	1057	1085	1002	1037	869	869	955	967	1058	1090
1046	943	996	990	970	1040	998	1032	1260	1190	1200	1150	1160
1030	970	925	1150	1117	940	1022	916	964	1040	1088	960	940
1092	1046	1025	1054	960	1066	1041	1060	1082	1067	997	990	1017
971	1200	1100	1100	1080	980	1072	1044	1000	980	1100	1170	1117
1014	976	911	1150	978	972	1000	1093	885	940	1130	1100	904
1200	1087	920	1098	1080	950	1056	1100	1150	1120	900	925	1100
1250	1246	1192	1196	1182	1230	1216	1292	1195	1218	1300	1247	1118
1090	1046	1010	1054	913	1066	1030	1060	1082	1063	978	977	1017
1099	1066	1207	1151	1056	1118	1116	1112	1171	1199	1083	1151	1159
1010	980	960	1060	980	968	993	1066	890	930	1060	1111	940
1033	980	930	1153	1111	945	1025	920	970	1045	1090	967	945
1202	1206	1140	1200	1160	1200	1185	1300	1298	1204	1304	1270	1111
1100	1016	1051	1091	1047	1059	1061	1139	913	946	1108	1044	1058
991	1021	1056	993	1062	1032	1026	1046	1018	990	1016	950	971
1060	1040	1004	1052	910	1060	1021	1064	1082	1070	980	979	1014
988	1203	1101	1102	1088	978	1077	1046	1004	987	1102	1178	1119
1085	1050	999	1062	1088	1020	1051	920	928	990	980	1066	1100
1109	1029	1060	1100	1060	1067	1071	1100	950	980	1106	1070	1069
1004	975	1060	1055	985	960	1007	1055	900	950	1054	1080	940
1004	980	1260	1130	1020	990	1064	1033	1200	1190	1204	1136	1160
992	1022	1055	995	1065	1031	1027	1044	1011	999	1011	945	970
1248	1230	1192	1198	1190	1232	1215	1293	1198	1220	1302	1253	1120
1033	975	939	1145	1119	945	1026	917	970	1045	1090	970	945
1202	1206	1145	1190	1160	1200	1184	1260	1298	1206	1304	1270	1109
1092	1048	1025	1053	985	1066	1045	1060	1082	1067	999	990	1017
1015	980	910	1054	979	975	986	1090	890	945	1120	1096	900
1035	985	935	1104	1102	944	1018	923	980	1046	1098	970	960
1211	1089	925	1100	1082	952	1060	1102	1153	1129	903	924	1102
1110	1080	1202	1152	1070	1120	1122	1112	1171	1210	1086	1152	1159

A AVG	AVG TOTAL	BAS	BA	BAL	BIS	BI	BIL	B AVG	MAS	MA	MAL	MIS
968	994	49	43	51	53	56	49	50	50	48	49	53
1165	1053	32	41	46	47	39	50	43	51	47	36	47
985	991	41	48	41	42	51	43	44	42	46	44	53
1036	1031	48	44	46	50	49	50	48	46	49	50	49
1069	1064	49	52	48	51	64	48	52	46	48	52	45
1009	1001	47	40	54	49	54	46	48	48	54	51	52
1049	1053	47	55	56	47	53	55	52	53	53	45	54
1228	1213	51	51	52	45	56	47	50	58	55	55	49
1030	1024	47	44	46	50	48	50	48	46	49	49	49
1146	1131	67	42	46	50	47	48	50	55	47	48	51
1000	997	48	41	55	50	55	47	49	47	55	51	53
990	995	42	49	42	43	52	44	45	42	45	45	54
1248	1193	52	52	53	37	56	43	49	58	55	55	49
1035	1073	54	48	52	56	53	55	53	57	57	52	57
999	1010	48	52	49	50	51	44	49	48	49	47	45
1032	1021	46	43	45	49	49	49	47	46	48	47	48
1073	1068	50	53	49	52	65	49	53	46	49	53	46
997	1014	50	44	52	54	56	50	51	51	50	48	53
1046	1081	55	49	53	57	54	56	54	57	57	53	58
997	998	49	40	52	49	53	48	49	43	51	49	52
1154	1075	36	43	47	49	41	52	45	53	49	42	49
997	1008	49	51	50	50	52	45	50	49	50	48	46
1231	1214	52	53	54	46	57	48	52	58	56	56	50
990	996	42	49	42	43	52	44	45	43	47	45	54
1241	1191	52	52	53	55	56	44	52	58	55	57	49
1036	1034	45	44	47	50	49	50	48	47	49	50	49
1007	995	46	41	53	48	53	44	48	47	53	50	50
996	996	43	50	43	44	53	45	46	43	46	43	55
1052	1056	48	56	57	48	54	56	53	54	54	46	55
1148	1136	68	43	47	51	48	49	51	56	48	49	52

MI	MIL	M AVG	AAS	AA	AAL	AIS	AI	AIL	A AVG	AVG TOTAL
47	42	48	53	56	53	50	49	53	52	50
47	48	46	70	57	50	45	42	52	53	47
44	34	44	48	48	49	46	48	38	46	45
48	43	48	50	49	55	49	50	48	50	49
40	53	47	60	65	72	68	80	80	71	57
42	49	49	53	57	58	53	45	39	51	50
55	42	50	59	65	57	58	59	50	58	54
46	48	52	59	54	56	58	53	48	55	52
47	39	47	50	49	55	47	50	43	49	48
60	53	52	53	60	58	49	44	43	51	51
42	50	50	54	58	59	54	47	40	52	50
45	36	45	49	49	50	47	49	39	47	46
46	48	52	59	54	56	58	53	48	55	52
56	58	56	56	59	59	56	62	59	59	56
48	44	47	46	50	51	49	48	48	49	48
46	38	46	49	48	54	46	49	44	47	45
42	54	48	61	66	73	69	81	82	72	58
49	43	49	54	57	54	51	50	52	53	51
57	59	57	57	59	59	56	64	60	59	57
41	49	48	50	51	48	52	46	41	48	48
49	50	49	69	58	53	48	44	54	56	50
49	46	48	47	51	52	50	49	49	50	49
47	49	53	60	55	57	59	54	49	56	53
45	35	45	49	49	50	47	49	39	47	46
47	48	52	59	54	56	58	53	49	55	53
48	44	48	50	49	55	50	50	48	50	49
41	48	48	52	56	57	52	44	38	50	49
46	37	45	49	50	51	47	49	40	48	46
56	43	51	60	66	58	59	60	51	59	55
61	54	53	54	61	59	50	45	44	52	52

Master Chart **Sheet B**

Age	Sex	Ht (cm)	Wt (kg)	BMI	BSA	PRO BNP	HB	CR	TSH	HTN	DM
56	M	166	72	26.1	1.80		12.9	0.9	3.4	0	1
61	F	155	71	29.6	1.70		13	0.7	4.7	0	0
55	F	146	62	29.1	1.54		13	0.8	2.9	0	0
56	F	148	54	24.7	1.47		12.9	0.9	1.8	1	0
64	F	150	55	24.4	1.49		13	0.9	2.2	0	0
55	F	152	54	23.4	1.49		12.8	0.8	3.8	0	0
54	M	172	62	21.0	1.73		12	0.8	4.8	0	1
62	F	156	69	28.4	1.69		14	0.8	4.9	0	0
66	F	151	65	28.5	1.61		13.7	0.9	2.5	1	0
59	M	166	59	21.4	1.65		14	1	3.3	0	0
65	F	156	65	26.7	1.65		13.7	1	3.8	0	0
57	F	148	58	26.5	1.51		12.8	1.1	2.5	0	0
49	F	146	53	24.9	1.44		12.9	0.7	1.9	0	0
63	F	148	54	24.7	1.47		13	0.65	2.2	0	0
70	F	146	54	25.3	1.45		13	0.6	1.9	0	0
54	M	165	71	26.1	1.78		13	0.55	2	1	1
62	F	154	71	29.9	1.69		12.8	0.56	2.3	0	0
62	F	145	62	29.5	1.53		12.7	0.9	2.2	0	0
55	F	149	54	24.3	1.47		13	1	2.8	0	0
65	F	149	55	24.8	1.48		13.4	1	2.6	0	0
56	F	151	55	24.1	1.50		13.6	0.8	3.2	0	0
56	M	170	69	23.9	1.80		13.6	1.1	3.3	0	0
76	F	155	69	28.7	1.68		13.9	1.3	3.3	1	0
65	F	152	64	27.7	1.61		14	0.75	3	0	0
66	M	166	59	21.4	1.65		13	0.8	3.8	0	0
65	F	155	65	27.1	1.64		12.9	0.8	3.2	0	0
69	F	148	59	26.9	1.52		13	0.9	3.2	0	0
51	F	147	53	24.5	1.45		13	1.1	3.6	0	0
63	F	148	55	25.1	1.48		13.2	1.33	3.5	0	0
71	F	146	56	26.3	1.47		13.4	1.2	3.2	0	0

HYPO T4	COPD	CAD	DYSLIPID	OBESITY	OSA	F/H/O CAD	HX COVID	INDEX EVENT
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	2	0	0	0	0
0	0	0	0	2	0	0	0	0

SOB	**FC**	**PND**	COUGH	EXPECTOR	ANASARCA	OLIGURIA	ANGINA	PALPIT	SYNCOPE	SGLT2I
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	1	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	1	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	1	0	0
0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0

Loop Diuretic	Frusemide equivalent dose /day	MRA	Dose/ day	PR	PULSE CHAR	SBP	DBP	HTN @VISIT	RR	Sat RA %	JVP	RALES	
0				64	0			0	12	98	0	0	
0				76	0			0	13	99	0	0	
0				65	0			0	12	99	0	0	
0				87	0			0	13	100	0	0	
0				67	0			0	12	100	0	0	
0				76	0			0	14	99	0	0	
0				82	0			0	12	98	0	0	
0				76	0			0	12	97	0	0	
0				65	0			0	12	99	0	0	
0				75	0			0	12	98	0	0	
0				68	0			0	12	99	0	0	
0				88	0			0	12	100	0	0	
0				75	0			0	12	99	0	0	
0				88	0			0	14	99	0	0	
0				90	0			0	13	99	0	0	
0				66	0			0	13	99	0	0	
0				72	0			0	13	99	0	0	
0				68	0			0	12	99	0	0	
0				85	0			0	13	99	0	0	
0				77	0			0	12	100	0	0	
0				76	0			0	13	100	0	0	
0				82	0			0	13	100	0	0	
0				80	0			0	14	97	0	0	
0				65	0			0	13	98	0	0	
0				80	0			0	12	97	0	0	
0				77	0			0	13	98	0	0	
0				88	0			0	13	98	0	0	
0				75	0			0	12	99	0	0	
0				88	0			0	12	99	0	0	
0				90	0			0	13	99	0	0	

S1	LOUD P2	GALLOP	MURMUR	OUTPUT	PED EDEMA	SR	LAE	PR	QRS AXIS	QRSD
0	0	0	0	0	0	1	0	150	40	70
0	0	0	0	0	0	1	0	140	60	65
0	0	0	0	0	0	1	0	160	65	70
0	0	0	0	0	0	1	0	136	70	72
0	0	0	0	0	0	1	0	144	48	65
0	0	0	0	0	0	1	0	120	70	77
0	0	0	0	0	0	1	0	140	45	66
0	0	0	0	0	0	1	0	146	20	70
0	0	0	0	0	0	1	0	150	30	70
0	0	0	0	0	0	1	0	144	50	65
0	0	0	0	0	0	1	0	150	46	70
0	0	0	0	0	0	1	0	158	30	68
0	0	0	0	0	0	1	0	154	0	70
0	0	0	0	0	0	1	0	150	20	66
0	0	0	0	0	0	1	0	180	50	70
0	0	0	0	0	0	1	0	154	45	70
0	0	0	0	0	0	1	0	150	70	72
0	0	0	0	0	0	1	0	180	65	70
0	0	0	0	0	0	1	0	136	60	72
0	0	0	0	0	0	1	0	144	50	65
0	0	0	0	0	0	1	0	148	70	80
0	0	0	0	0	0	1	0	146	45	66
0	0	0	0	0	0	1	0	160	15	70
0	0	0	0	0	0	1	0	150	30	70
0	0	0	0	0	0	1	0	146	50	70
0	0	0	0	0	0	1	0	150	80	70
0	0	0	0	0	0	1	0	158	30	70
0	0	0	0	0	0	1	0	154	0	70
0	0	0	0	0	0	1	0	160	20	66
0	0	0	0	0	0	1	0	180	50	76

QTC	LVH	ST T CHANGES	CE	CTR %	LAE	Carinal angle	PVH GRADE	PAH	LUN FIELD ABN	**LVID D**	**LVID S**	**IVS D**	**IVS S**
386	0	0	0	45	0	67	0	0	0	44	25	11	13
402	0	0	0	44	0	68	0	0	0	39	27	8	9
420	0	0	0	47	0	70	0	0	0	43	30	10	11
422	0	0	0	46	0	66	0	0	0	44	24	9	12
366	0	0	0	48	0	68	0	0	0	40	20	10	12
362	0	0	0	42	0	65	0	0	0	41	21	8	11
386	0	0	0	46	0	65	0	0	0	38	22	9	10
400	0	0	0	48	0	67	0	0	0	40	27	8	10
398	0	0	0	49	0	69	0	0	0	44	25	8	10
380	0	0	0	44	0	70	0	0	0	46	27	8	11
396	0	0	0	47	0	65	0	0	0	43	26	8	11
390	0	0	0	48	0	70	0	0	0	36	20	8	11
397	0	0	0	50	0	69	0	0	0	48	28	9	11
378	0	0	0	50	0	69	0	0	0	41	22	8	11
400	0	0	0	50	0	70	0	0	0	43	23	9	11
390	0	0	0	46	0	67	0	0	0	45	27	11	13
390	0	0	0	48	0	69	0	0	0	40	27	8	9
410	0	0	0	47	0	71	0	0	0	45	30	10	11
422	0	0	0	46	0	66	0	0	0	45	24	9	12
366	0	0	0	48	0	68	0	0	0	42	22	10	12
364	0	0	0	47	0	68	0	0	0	44	28	8	11
386	0	0	0	46	0	65	0	0	0	38	24	9	10
404	0	0	0	48	0	69	0	0	0	42	30	8	10
398	0	0	0	49	0	69	0	0	0	44	25	8	10
400	0	0	0	44	0	70	0	0	0	46	27	8	11
400	0	0	0	48	0	67	0	0	0	44	26	8	11
404	0	0	0	48	0	70	0	0	0	38	22	8	11
397	0	0	0	50	0	69	0	0	0	45	30	9	11
386	0	0	0	50	0	69	0	0	0	41	26	8	11
400	0	0	0	48	0	70	0	0	0	43	25	9	11

PWD	PWS	LV mass	LV mass in	LV mass Th	LVMI Th	RWT	HYPERTR	ECHO LVH	RVID	EF	FS	LA PLAX
9	11	147.8	82.1	139	77	0.41	N	0	17	59	43	32
8	9	89.7	52.7	89	52	0.41	N	0	16	69	31	33
8	11	123.3	80.1	119	77	0.37	N	0	18	59	30	32
9	12	128.0	87.3	123	84	0.41	N	0	16	75	45	35
7.5	11	105.5	70.7	103	69	0.38	N	0	16	80	50	36
8	10	97.3	65.1	96	64	0.39	N	0	25	80	49	30
9	11	101.1	58.3	99	57	0.47	CR	0	23	60	42	28
8	10	93.5	55.3	92	55	0.40	N	0	22	61	33	35
9	11	118.6	73.7	115	71	0.41	N	0	21	58	43	32
8	11	117.9	71.3	115	69	0.35	N	0	20	71	41	36
8	11	105.3	63.9	103	63	0.37	N	0	20	69	40	34
8	11	78.8	52.1	79	53	0.44	CR	0	19	68	44	28
9	11	147.8	102.6	140	97	0.38	N	0	21	64	42	31
8	10	97.3	66.4	96	65	0.39	N	0	20	77	46	33
9	11	123.3	85.0	119	82	0.42	N	0	21	76	47	35
9	11	153.3	86.0	143	80	0.40	N	0	18	69	40	33
8	9	93.5	55.1	92	55	0.40	N	0	16	61	33	34
8	11	132.8	86.7	127	83	0.36	N	0	20	62	33	33
9	12	132.8	90.2	127	86	0.40	N	0	16	76	47	36
8	11	118.7	79.9	115	77	0.38	N	0	18	80	48	36
8	10	109.4	73.0	107	71	0.36	N	0	24	66	36	30
9	11	101.1	56.2	99	55	0.47	CR	0	22	66	37	30
8	10	101.3	60.2	99	59	0.38	N	0	22	57	29	36
9	11	118.6	73.8	115	71	0.41	N	0	21	58	43	33
8	11	117.9	71.3	115	69	0.35	N	0	20	71	41	36
8	11	109.4	66.7	107	65	0.36	N	0	20	70	41	35
9	11	93.4	61.3	93	61	0.47	CR	0	19	72	42	30
9	11	132.8	91.8	127	88	0.40	N	0	21	62	33	33
8	10	97.3	65.9	96	65	0.39	N	0	21	66	37	34
9	11	123.3	83.6	119	80	0.42	N	0	21	71	42	35

LA A4 C L	LA A4 C W	LA V	LAV I	LA E	A o	RWM A	MV E	MV A	EDT	L wave	LAT E'	LAT E/E'
49	31	25.4	14.1	0	23	0	0.9	0.7	195	0	16	5.6
46	29	23.0	13.5	0	25	0	0.8	0.6	220	0	20	4.0
46	30	23.1	15.0	0	29	0	1	0.7	240	0	15	6.7
48	34	29.9	20.4	0	30	0	0.7	0.5	220	0	18	3.9
56	35	36.9	24.7	0	29	0	1.1	0.9	214	0	13	8.5
50	30	23.5	15.7	0	24	0	0.76	0.5	220	0	13	5.8
51	30	22.4	12.9	0	25	0	0.74	0.72	190	0	12	6.2
51	35	32.7	19.3	0	28	0	0.9	0.7	186	0	15	6.0
50	30	25.1	15.6	0	29	0	1.1	0.7	210	0	12	9.2
52	36	35.2	21.3	0	30	0	0.9	0.7	200	0	15	6.0
50	40	35.6	21.6	0	29	0	0.8	0.6	180	0	16	5.0
49	29	20.8	13.8	0	24	0	0.84	0.63	210	0	14	6.0
52	36	30.4	21.1	0	34	0	0.9	0.8	220	0	12	7.5
29	33	16.5	11.3	0	28	0	0.62	0.86	210	0	10	6.2
50	34	31.1	21.4	0	29	0	1.1	0.9	210	0	12	9.2
52	34	30.5	17.1	0	29	0	1	0.7	196	0	15	6.7
49	32	27.9	16.5	0	25	0	0.9	0.6	220	0	19	4.7
48	31	25.7	16.8	0	29	0	1.1	0.8	224	0	14	7.9
50	35	32.9	22.4	0	31	0	0.8	0.6	220	0	16	5.0
54	35	35.6	24.0	0	29	0	1	0.9	210	0	12	8.3
51	30	24.0	16.0	0	24	0	0.78	0.52	210	0	14	5.6
54	34	28.8	16.0	0	26	0	0.75	0.7	198	0	13	5.8
48	35	31.6	18.8	0	28	0	1	0.7	188	0	14	7.1
48	30	24.9	15.5	0	29	0	1.1	0.7	210	0	12	9.2
50	36	33.9	20.5	0	30	0	0.9	0.7	200	0	15	6.0
49	40	35.9	21.9	0	29	0	0.9	0.67	186	0	15	6.0
50	29	22.8	14.9	0	24	0	0.89	0.7	200	0	15	5.9
50	36	31.1	21.5	0	32	0	0.9	0.8	220	0	13	6.9
49	33	28.8	19.5	0	29	0	0.76	0.86	210	0	11	6.9
49	34	30.5	20.7	0	29	0	1.1	0.9	190	0	13	8.5

MED E'	MED E/E'	AVG E/E'	LAT A'	MED A'	TR GRADE	TR GRAD	LVDD GRADE	TAPSE	AOV	PV	MR	AR
10	9.0	7.3	11	8	1	10	0	19	1	1	0	0
14	5.7	4.9	16	11	1	11	0	23	1	1	0	0
10	10.0	8.3	12	8	1	15	0	22	1	1	0	0
10	7.0	5.4	11	9	0	NA	0	23	1.1	0.9	0	0
13	8.5	8.5	11	10	1	12	0	21	1.3	0.9	1	0
12	6.3	6.1	10	9	1	12	0	20	1.3	1.2	0	0
10	7.4	6.8	11	9	0	NA	0	18	0.85	0.7	0	0
12	7.5	6.8	13	10	1	16	0	21	1	1	0	0
9	12.2	10.7	9	6	1	20	0	22	1.2	0.9	1	0
9	10.0	8.0	12	6	1	21	0	22	1	1	1	0
13	6.2	5.6	12	10	1	12	0	21	1	1	0	0
10	8.4	7.2	12	8	0	NA	0	18	1.5	1.2	0	0
8	11.3	9.4	10	6	0	NA	0	19	1.2	1.1	0	0
10	6.2	6.2	11	11	1	12	0	24	1.2	0.9	0	0
8	13.8	11.5	10	6	1	18	0	21	1	1	0	0
10	10.0	8.3	11	8	1	11	0	20	1	1	0	0
13	6.9	5.8	14	10	1	11	0	24	1	1	0	0
11	10.0	8.9	11	7	1	16	0	23	1.1	0.9	0	0
10	8.0	6.5	10	9	0	NA	0	24	1.1	1	0	0
11	9.1	8.7	10	9	1	14	0	22	1.1	0.9	1	0
12	6.5	6.0	11	9	1	13	0	20	1.3	1.2	0	0
11	6.8	6.3	10	8	0	NA	0	20	0.9	0.9	0	0
11	9.1	8.1	10	7	1	18	0	24	1	1	0	0
9	12.2	10.7	9	6	1	20	0	22	1.2	0.9	1	0
9	10.0	8.0	12	6	1	21	0	22	1	1	1	0
12	7.5	6.8	12	10	1	14	0	21	1.1	0.9	0	0
10	8.9	7.4	12	8	0	NA	0	18	1.5	1.2	0	0
8	11.3	9.1	10	6	0	NA	0	21	1.2	1.1	0	0
9	8.4	7.7	9	8	1	16	0	24	1.2	0.9	0	0
9	12.2	10.3	9	7	1	19	0	21	1	1	0	0

AS	PE	GLS ABN	BAS	BA	BAL	BIS	BI	BIL	MAS	MA	MAL	MIS
0	0	0	19	21	17	17	17	18	20	19	19	17
0	0	0	22	23	26	23	18	22	24	24	24	29
0	0	0	21	21	23	22	19	17	22	21	22	20
0	0	0	21	23	25	23	24	25	30	26	24	27
0	0	0	22	23	25	21	25	26	30	26	25	27
0	0	0	21	19	22	21	23	24	23	23	25	21
0	0	0	25	24	23	24	23	24	24	27	26	27
0	0	0	21	21	22	21	19	23	24	21	25	20
0	0	0	19	21	17	19	20	21	19	20	21	24
0	0	0	23	24	23	25	21	24	26	27	25	29
0	0	0	24	19	21	22	21	21	19	21	23	21
0	0	0	21	23	23	24	23	21	24	25	26	24
0	0	0	23	20	18	19	17	22	21	22	20	20
0	0	0	19	21	22	28	21	23	24	26	28	26
0	0	0	19	18	17	18	19	17	21	22	21	23
0	0	0	20	21	18	18	18	18	20	19	19	20
0	0	0	23	24	26	23	19	22	24	24	24	29
0	0	0	21	24	23	22	20	18	22	21	22	21
0	0	0	22	23	24	23	24	26	29	27	24	27
0	0	0	23	23	26	22	24	26	23	26	25	27
0	0	0	22	21	22	21	23	23	23	23	25	22
0	0	0	26	22	23	24	24	24	23	27	26	28
0	0	0	21	22	22	21	19	23	23	21	25	20
0	0	0	19	21	17	19	20	21	19	20	21	24
0	0	0	23	24	23	25	21	24	26	27	25	29
0	0	0	26	20	21	22	23	21	20	25	26	21
0	0	0	21	23	24	24	23	21	24	30	26	24
0	0	0	23	22	19	19	17	22	21	22	21	20
0	0	0	21	21	22	28	21	23	24	26	28	26
0	0	0	19	18	18	18	20	17	21	22	21	23

MI	MIL	AAS	AA	AAL	AIS	AI	AIL
18	17	18	17	17	19	22	17
17	19	25	29	24	29	28	17
19	19	24	28	26	26	24	26
25	28	36	31	29	33	27	32
27	28	33	33	30	33	28	30
21	23	26	28	29	31	28	27
19	21	24	25	21	23	31	32
20	19	23	22	21	26	24	23
26	26	24	27	26	25	20	22
25	26	31	29	32	32	34	29
23	26	25	25	26	27	26	28
24	23	26	27	29	25	24	27
19	19	18	23	24	22	23	22
28	20	30	31	28	28	28	29
21	23	22	24	25	26	25	24
21	21	20	20	20	22	22	25
19	20	25	29	24	29	28	21
19	19	24	28	26	26	24	26
25	27	34	31	29	32	27	32
27	28	33	32	31	33	29	30
21	23	26	28	29	32	28	28
20	21	24	26	21	23	31	32
20	20	23	22	22	26	25	23
26	26	24	27	26	25	20	22
25	26	31	29	32	32	34	29
23	26	27	28	29	27	28	28
24	24	26	27	29	25	26	27
19	21	20	23	24	22	23	22
28	21	30	31	28	28	29	29
22	23	22	24	25	26	25	24

LVIDD	LVIDS	IVSD	IVSS	PWD	PWS	RVID	LV mass dias	LV mass index	LA 4c L	LA 4c W
46	24	13	16	10	12	41	75	41.7	50	40
56	47	13	15	6	8	39	89	52.3	52	48
49	36	7	10	6	8	33	94	61.1	43	36
50	42	9	12	7	12	35	91	62.1	47	40
39	20	7	13	5	14	39	46	30.8	46	40
40	20	6	10	5	10	38	46	30.8	46	35
52	25	9	12	6	16	39	77	44.4	48	37
41	25	6	9	5	11	37	46	27.2	37	36
41	20	10	14	5	12	39	74	46.0	40	36
41	25	6	9	5	11	37	46	27.8	37	36
46	18	11	14	8	17	35	75	45.5	36	45
54	36	6	10	6	10	46	60	39.7	43	51
41	28	9	14	6	12	30	77	53.5	40	36
47	20	7	10	5	9	38	70	47.8	40	39
51	20	7	13	7	12	35	94	64.8	39	46
49	25	7	13	5	10	36	75	42.1	43	35
51	29	7	10	6	13	38	55	32.5	45	29
52	25	9	12	6	16	39	77	50.3	48	37
46	25	6	12	6	10	41	60	40.7	47	44
57	33	10	14	9	16	43	85	57.3	51	44
43	27	7	11	5	8	41	57	38.0	40	44
41	28	9	14	6	12	30	77	42.8	40	36
47	20	7	10	5	9	38	70	41.6	40	39
51	20	7	13	7	12	35	94	58.5	39	46
49	25	7	13	5	10	36	75	45.3	43	35
51	29	7	10	6	13	38	55	33.5	45	29
52	25	9	12	6	16	39	77	50.6	48	37
46	25	6	12	6	10	41	60	41.5	47	44
57	33	10	14	9	16	43	85	57.5	51	44
43	27	7	11	5	8	41	57	38.7	40	44

LA	LAV	LAVI	AO	LV ED Vol	LV ED vol index	LV ES vol	LV ES vol index	LV SV	LV SV INDEX	LV CO	LV CO INDEX	LV EF
42	44	24	27	75	41	20	11	54	30	4.8	2.7	73
40	52	31	27	67	39	17	10	50	30	7.4	4.3	75
41	33	22	27	91	59	26	17	65	42	5.5	3.6	71
30	29	20	27	88	60	49	34	38	26	5.7	3.9	44
41	39	26	27	122	82	46	31	76	51	3.1	2.1	62
35	29	20	27	94	63	24	16	70	47	3.8	2.5	74
43	40	23	27	69	40	17	10	51	30	5.8	3.3	75
30	21	12	27	101	60	47	28	54	32	3.8	2.2	53
34	26	16	27	71	44	25	16	46	29	4.4	2.7	65
30	21	13	27	101	61	47	29	54	33	3.8	2.3	53
39	33	20	27	94	57	30	18	64	39	4.1	2.5	68
40	46	30	27	96	63	26	17	69	46	4.1	2.7	73
37	28	19	27	111	77	48	34	63	43	4.7	3.3	56
44	36	24	27	89	60	30	21	58	40	5.3	3.6	66
43	40	28	27	70	48	26	18	44	30	5.7	3.9	63
44	35	19	27	88	49	28	16	60	34	4.9	2.8	68
33	23	13	27	90	53	29	17	61	36	4	2.4	68
43	40	26	27	69	45	17	11	51	33	5.8	3.8	75
38	41	28	27	70	48	25	17	46	31	4.5	3.1	65
42	49	33	27	84	57	27	18	58	39	5.2	3.5	68
40	37	25	27	65	44	19	13	46	31	4.7	3.1	70
37	28	15	27	111	62	48	27	63	35	4.7	2.6	56
44	36	21	27	89	53	30	18	58	35	5.3	3.2	66
43	40	25	27	70	44	26	16	44	27	5.7	3.5	63
44	35	21	27	88	53	28	17	60	36	4.9	3.0	68
33	23	14	27	90	55	29	18	61	37	4	2.4	68
43	40	26	27	69	45	17	11	51	34	5.8	3.8	75
38	41	28	27	70	48	25	17	46	31	4.5	3.1	65
42	49	33	27	84	57	27	18	58	39	5.2	3.5	68
40	37	25	27	65	44	19	13	46	31	4.7	3.2	70

RV ED VOL	RV ED VOL INDEX	RV ES VOL	RV ES VOL INDEX	RV STROKE VOL	RV STROKE VOL INDEX	RV CO	RV CO INDEX	RV EF
139	77.2	55	30.6	84	46.7	4.8	2.7	60
199	116.9	84	49.3	115	67.5	7.4	4.3	58
119	77.3	41	26.6	78	50.7	5	3.2	66
135	92.1	55	37.5	80	54.6	5.7	3.9	59
77	51.6	36	24.1	41	27.5	2.8	1.9	53
94	62.9	40	26.8	54	36.1	3.8	2.5	57
127	73.3	49	28.3	78	45.0	5.8	3.3	61
94	55.6	40	23.7	54	32.0	3.8	2.2	57
117	72.7	48	29.8	69	42.9	4.4	2.7	59
94	56.8	40	24.2	54	32.6	3.8	2.3	57
83	50.4	43	26.1	40	24.3	4	2.4	48
143	94.6	67	44.3	76	50.3	4.1	2.7	53
108	75.0	43	29.9	65	45.1	4.7	3.3	60
118	80.5	37	25.2	81	55.3	5.4	3.7	69
143	98.5	39	26.9	104	71.7	5.8	4.0	73
132	74.1	28	15.7	104	58.4	4.9	2.8	79
118	69.6	53	31.3	65	38.4	3.9	2.3	55
127	82.9	49	32.0	78	50.9	5.8	3.8	61
120	81.5	39	26.5	81	55.0	5	3.4	68
178	119.9	77	51.9	101	68.0	5.3	3.6	57
104	69.4	53	35.4	51	34.0	4.8	3.2	49
108	60.0	43	23.9	65	36.1	4.7	2.6	60
118	70.1	37	22.0	81	48.2	5.4	3.2	69
143	89.0	39	24.3	104	64.7	5.8	3.6	73
132	79.8	28	16.9	104	62.9	4.9	3.0	79
118	72.0	53	32.3	65	39.6	3.9	2.4	55
127	83.4	49	32.2	78	51.2	5.8	3.8	61
120	82.9	39	27.0	81	56.0	5	3.5	68
178	120.5	77	52.1	101	68.4	5.3	3.6	57
104	70.6	53	36.0	51	34.6	4.8	3.3	49

BAS	BA	BAL	BIS	BI	BIL	B AVG	MAS	MA	MAL	MIS	MI	MIL	M AVG
1002	1033	1028	1041	1002	1002	1018	1031	1028	1033	1021	1015	1041	1028
1015	1012	1031	993	1012	1012	1013	1029	1031	1012	1015	1004	993	1014
1032	1002	1029	1002	1033	1033	1022	1017	1002	1002	1004	1033	1002	1010
1034	1004	1017	1015	1012	1012	1016	1002	1025	1004	1040	1004	1015	1015
1040	1006	1002	1032	1002	1002	1014	1012	1043	1006	1037	1006	1032	1023
1028	1034	1012	1034	1002	1004	1019	1033	1010	1034	1037	1040	1034	1031
1031	1002	1033	1040	1012	1006	1021	1012	993	1002	1041	1004	1040	1015
1029	1025	1012	1028	1033	1006	1022	1002	1002	1025	1012	1006	1028	1013
1017	1010	1002	1031	1012	1034	1018	1004	1015	1043	1002	1034	1031	1022
1002	1041	1004	1002	1002	1002	1009	1006	1021	1021	1004	1002	1006	1010
1012	989	1006	1025	1004	1025	1010	1040	1015	1015	1006	1025	1034	1023
1033	1021	1040	1043	1006	1043	1031	1004	1004	1002	1040	1043	1002	1016
1012	1015	1037	1010	1034	1010	1020	1006	1040	1012	1037	1021	1025	1024
1002	1004	1037	993	1002	1041	1013	1034	1037	1033	1037	1015	1043	1033
1004	1040	1041	1002	1025	989	1017	1002	1037	1012	1041	1034	1021	1025
1006	1037	993	1015	1043	1021	1019	1025	1041	1002	993	1002	1015	1013
1034	1037	1002	1032	1021	1015	1024	1043	993	1004	1002	1012	1004	1010
1002	1041	1015	1034	1015	1004	1019	1021	1002	1006	1015	1033	1040	1020
1025	993	1032	1040	1004	1033	1021	1015	1015	1040	1032	1012	1037	1025
1043	1002	1034	1028	1040	1012	1027	1004	1032	1037	1034	1002	1037	1024
1010	1015	1040	1031	1037	1002	1023	1040	1034	1037	1040	1004	1041	1033
1041	1032	1028	1002	1037	1004	1024	1037	1040	1041	1028	1006	993	1024
989	1034	1031	1004	1041	1006	1018	1037	1028	993	1031	1006	1037	1022
1021	1040	1002	1006	993	1040	1017	1041	1031	1002	1002	1034	1041	1025
1015	1028	1004	1034	1002	1037	1020	993	1002	1015	1037	1002	993	1007
1004	1031	1006	1034	1015	1037	1021	1037	1025	1032	1037	1025	1002	1026
1040	1002	1034	1040	1032	1041	1032	1041	1043	1034	1041	1043	1028	1038
1037	1025	1002	1028	1034	993	1020	993	1002	1040	1012	1010	1031	1015
1037	1043	1025	1031	993	1002	1022	1002	1012	1028	1002	1041	1002	1015
1041	1010	1025	1029	1002	1015	1020	1015	1033	1031	1004	989	1004	1013

AAS	AA	AAL	AIS	AI	AIL	A AVG	AVG TOTAL	BAS	BA	BAL
1017	1010	1004	1025	1025	993	1012	1020	50	52	49
1002	993	1006	1010	1043	1002	1009	1012	51	50	54
1012	1002	1034	1041	1021	1015	1021	1018	48	51	53
1033	1015	1002	989	1015	1032	1014	1015	54	48	52
1012	1032	1037	1021	1002	1034	1023	1020	54	51	51
1002	1034	1041	1015	1012	1040	1024	1025	49	53	51
1004	1040	993	1004	1033	1028	1017	1018	50	48	52
1006	1028	1002	1040	1012	1031	1020	1018	49	49	53
1034	1031	1015	1037	1002	1002	1020	1020	52	49	52
1002	1002	1032	1037	1004	1025	1017	1012	51	49	53
1025	1004	1034	1041	1006	1043	1026	1019	48	49	53
1043	1012	1040	1002	1040	1002	1023	1023	48	49	54
1010	1002	1028	1004	1037	1012	1016	1020	52	49	49
1006	1004	1031	1040	1037	1033	1025	1024	54	49	54
1040	1006	1002	1037	1034	1006	1021	1021	51	49	51
1037	1040	1037	1040	1002	1034	1032	1021	51	49	48
1037	1004	1037	1028	1025	1002	1022	1018	50	49	50
1041	1006	1041	1031	1043	1025	1031	1023	51	49	51
993	1034	1012	1002	1010	1043	1016	1021	50	49	52
1002	1002	1002	1025	1006	1021	1010	1020	48	49	49
1015	1025	1002	1043	1040	1034	1027	1027	53	49	54
1032	1043	1015	1010	1037	1002	1023	1024	52	49	49
1034	1021	1032	993	1037	1025	1024	1021	49	49	51
1040	1015	1034	1002	1041	1043	1029	1024	53	49	52
1028	1004	1040	1032	993	1021	1020	1016	50	49	51
1031	1040	1028	1034	1002	1015	1025	1024	52	49	53
1002	1040	1031	1040	1002	1034	1025	1032	48	49	48
1006	1037	1002	1028	1004	1002	1013	1016	52	49	49
1034	1037	1004	1031	1006	1012	1021	1019	48	49	54
1002	1031	1010	1006	1034	1033	1019	1017	49	49	51

BIS	BI	BIL	B AVG	MAS	MA	MAL	MIS	MI	MIL	M AVG	AAS	AA
54	48	52	51	52	54	52	48	48	54	51	51	53
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48	51	49	50	54	48	52	50	48	52	51	52	53
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AAL	AIS	AI	AIL	A AVG	AVG TOTAL
53	49	50	51	51	51
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49	52	49	53	51	51
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51	52	48	54	52	51
49	49	53	48	50	51