Effect of Aerobic Interval Training in improving functional capacity and LV remodelling in post-MI patients - a Randomized Controlled Trial

Dissertation submitted to the Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu in partial fulfillment of the requirement for the MD branch XIX (Physical Medicine and Rehabilitation) University Examination in May 2020

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DECLARATION

I hereby certify that the dissertation titled " Effect of Aerobic Interval Training (AIT) in improving functional capacity and LV remodelling in post-MI Patients- a Randomized Controlled Trial " is my bonafide work in partial fulfillment of the requirement of the Tamil Nadu Dr. MGR University, Chennai, for the MD branch XIX (Physical Medicine and Rehabilitation) for university examinations in May 2020.

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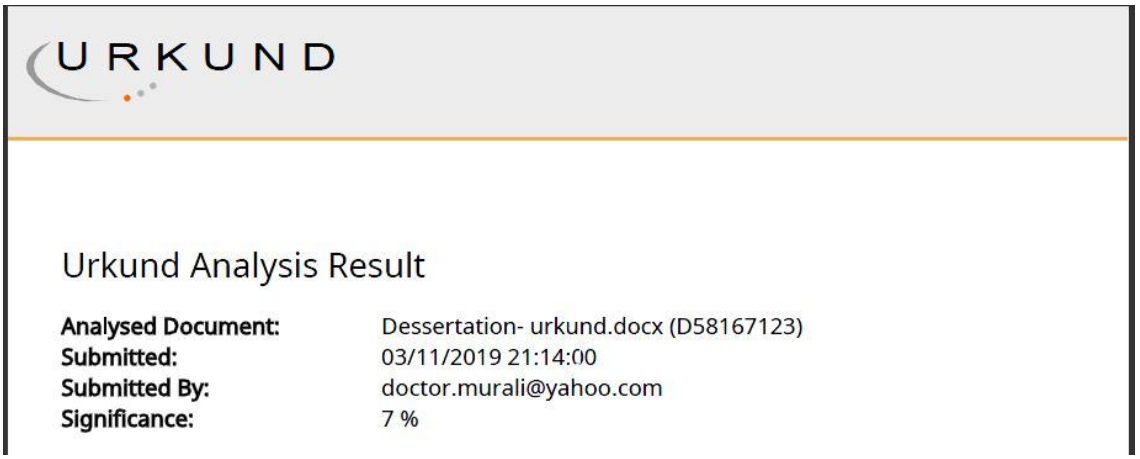
Anti-Plagiarism Certificate



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Acknowledgements

I would like to thank Dr George Tharion and Dr Oommen George my guides, for helping me throughout the course of this study, and being the constant source of motivation and encouragement at each step of the journey.

My sincere gratitude to my co-guide, Dr Sujith Thomas Chacko, Dr Anoop Alex, Dr Paul George, Dr Viji Thomson (Cardiology). Dr Bobeena Chandy (PMR), Dr Arun Jose Nellickal (Biochemistry) and Dr Gowri Sampath (Biostatistics) for their input and valuable guidance.

Many thanks to Cardiac Technicians- Sasi Rekha, Shalom, Princy, Priya, Priyanka, swarnim, Nithya, Viji, Reesa and Jeni, Physiotherapist Yasin, and Nursing staff- Clara J, Vani, and Glory for helping me throughout the study.

I am very thankful to all my patients who participated in this study

List of Abbreviations

6MWD	6 MINUTE WALK TEST
ACS	ACUTE CORONARY SYNDROME
ADL	ACTIVITIES OF DAILY LIVING
AIT	AEROBIC INTERVAL TRAINING
AMI	ACUTE MYOCARDIAL INFARCTION
BMI	BODY MASS INDEX
CABG	CORONARY ARTERY BYPASS GRAFT
CAD	CORONARY ARTERY DISEASE
CR	CARDIAC REHABILITATION
CRT	CARDIAC RESYNCHRONIZATION THERAPY
DBP	DIASTOLIC BLOOD PRESSURE
ECHO	ECHOCARDIOGRAM
EPOC	EXCESS POST-EXERCISE OXYGEN CONSUMPTION
HIIT	HIGH INTENSITY INTERVAL TRAINING
HRR	HEART RATE RECOVERY
HTN	HYPERTENSION
ICD	IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR
LV	LEFT VENTRICLE
LVEDV	LEFT VENTRICLE END DIASTOLIC VOLUME
LVEF	LEFT VENTRICLE EJECTION FRACTION
LVESV	LEFT VENTRICLE END SYSTOLIC VOLUME
LVGLS	LEFT VENTICLE GLOBAL LONGITUDINAL STRAIN
MCT	MODERATE CONTINUOUS TRAINING
METS	METABOLIC EQUIVALENTS
MHR	MAXIMUM HEART RATE
MPR	MAXIMUM PEAK HEART RATE
NSTEMI	NON-ST ELEVATION MYOCARDIAL INFARCTION
PCI	PERCUTANEOUS CORONARY INTERVENTION
RPE	RATE OF PERCEIVED EXERTION
RT	RESISTANCE TRAINING
RV TAPSE	RIGHT VENTRICLE TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSION
SBP	SYSTOLIC BLOOD PRESSURE
STEMI	ST ELEVATION MYOCARDIAL INFARCTION
VO2	VOLUME OF OXYGEN CONSUMPTION
WHR	WAIST HIP RATION

Table of Contents

1. ABSTRACT

Effect of Aerobic Interval Training (AIT) in improving functional capacity and Left Ventricle (LV) remodelling in post-Myocardial Infarction (MI) Patients- A Randomized Controlled Trial

1.1 Background:

Exercise-based cardiac rehabilitation aims to improve cardiac reserve and overall functional capacity in patients treated for acute coronary syndrome (ACS). Cardiac rehabilitation has been suggested to reverse pathological remodelling and improve LV stroke volume and Cardiac output. Over and above a primary Percutaneous Coronary Intervention (PCI) and drugs for post-Acute Myocardial Infarction (AMI) cardiac recovery, an exercise-based cardiac rehabilitation program has shown to improve mortality and morbidity in western studies. However, there is scarcity of data on the effectiveness of exercise-based cardiac rehabilitation on Reverse LV remodelling in post-MI Patients, in Indian setting.

1.2 Objectives:

To measure the effect of Aerobic Interval Training in improving functional capacity and LV remodelling in post-MI Patients who are medically stable at discharge

1.3 Methodology:

All adult participants who were less than 65 years, hospitalized for treatment of an acute coronary syndrome (ACS), once medically stable on optimal medical therapy and fit for discharge, were recruited for exercise-based cardiac rehabilitation program after

obtaining written consent. Participants were initially stratified based on the LV ejection fraction (EF<40%) into two groups and then randomized into intervention group and controls. Intervention group received a 12-week supervised AIT in addition to the standard post-AMI care whereas the controls received the standard post-AMI care as per the current institutional practice. Both the intervention group and the controls were assessed at baseline and at 3 months for (1) *Functional capacity*, as measured by the following variables - METS (Metabolic Equivalents), Heart rate recovery at 1 min (HRR) and 6min Walk Distance (6MWD) (2) *Cardiac function*, as measured by ECHO parameters and (3) *Cardiometabolic profile*, as assessed with the following variables - blood pressure, blood sugar, lipid profile, body mass index (BMI) and waist-hip ratio (WHR).

1.4 Results: 119 patients were randomized into 65 to receive AIT and 54 to receive the usual care. With a 53.8% drop-out in the AIT group, 30 completed the protocol while 42 among the control group completed the study. The exercise duration, METs achieved and 6-minute walk distance improved significantly in the AIT group. The treadmill-based Duke prognostic score also improved significantly in this group. The reduction in body weight and BMI was also significant among patients who underwent AIT. LV function (LVEF & LVGLS) showed significant improvement among intervention group with good compliance as compared to controls. However, the metabolic profile of patients did not show any significant difference between the two groups.

1.5 Conclusion: In post-MI patients who are medically stable on optimal medical therapy, aerobic interval training (AIT) leads to significant improvement in functional capacity and contributes to reverse LV remodelling, thus improving the cardiac prognosis

2. INTRODUCTION

Cardiac rehabilitation (CR), an important component in the continuum of care for individuals with cardiovascular disease, is a comprehensive multi-disciplinary intervention that is shown to reduce overall mortality and morbidity in patients with heart disease.

The main goals of CR are to limit the physiological and psychological effects of cardiac illness, reduce the risk for sudden death or re-infarction, control cardiac symptoms, stabilize or reverse the atherosclerotic process, and enhance the psychosocial and vocational status of selected patients. It achieves this through a multi-pronged strategy tailored to meet the individual and cultural needs of the patient and their family.

Core components of CR include medical evaluation followed by (a) participation in a structured prescribed exercise program, (b) dietary education to adopt a heart-healthy diet, (c) stress management, (d) cardiac risk factor modification, and (e) health education and counseling to ensure compliance to medication(1).

At Christian Medical College and Hospital, Vellore, all patients treated for the acute coronary syndrome are, educated on their cardiac status, the need for a healthy heart diet and the benefits of regular physical exercises. They are encouraged to continue their medications and lead a physically active lifestyle. Nevertheless, most post-MI patients are often seen to limit their physical activities for fear of a subsequent heart-attack and perhaps even death. Unfortunately, this may have a detrimental effect on long-term

cardiac prognosis.

The mortality rate among patients treated for ACS remains substantial despite the latest pharmacological and interventional therapies. Moller et al reported a mortality rate of > 25% among patients with an LVEF of 31-40% and < 15% among patients with LVEF > 50%, in the first two years following the MI. (2) Although meta-analysis of studies performed in the developed world demonstrated an added benefit with exercise-based CR, over and above the standard medical therapy, it is neither widely available nor taken up avidly by patients in India. Moreover, a lack of research data among patients in Indian settings may have a negative impact on even the physicians recommending an exercise-based structured cardiac rehabilitation program.

In this study effects of a supervised, centre-based, structured exercise-based CR program on all medically stable patients treated for an acute coronary syndrome were analyzed.

3. AIMS

To study the impact of Aerobic Interval Training (AIT) in improving cardiac function in post-MI patients receiving standard medical therapy.

4. OBJECTIVES OF THE STUDY

To measure the effect of Aerobic Interval Training in (a) improving functional capacity and (b) reversing LV remodelling in post-MI patients who are medically stable at discharge, on optimal medical therapy.

5. Review of Literature

5.1 What is Cardiac Rehabilitation?

Cardiac rehabilitation can be primary prevention, which includes risk factor modification and education before a cardiac event, or secondary prevention, which is cardiac rehabilitation after the onset of the cardiac disease which includes a comprehensive approach to improve functional capacity and risk factors reduction(1).

5.2 What are the phases of CR and their respective goals?

Cardiac rehabilitation typically comprises of four phases. The term phase is used to describe the varying time frames following a cardiac event. The secondary prevention component of CR requires delivery of exercise training, education and counselling, risk factor intervention and follow-ups

5.3 Phase I: Acute Phase/In-Hospital Cardiac Rehabilitation (2-5 days)

Goals:

- Assist the patient to identify personal Cardiovascular risk factors
- Prevention of deleterious effects of bed rest
- Discuss lifestyle modifications of personal risk factors and help provide an individual plan to support these lifestyle changes
- Gain support from family members to assist the patient in maintaining the necessary progress

- Plan a personal discharge activity programme and encourage the patient to adhere to home based exercise program
- Early mobilization-Passive range of movements, Active assisted ROM, Light activities with moderate assistance, ADL activities

  Walking 100 meters etc.
- Inform patients regarding phase II and phase III programs if available and encourage their attendance
- Pre discharge submaximal/symptom-limited exercise stress test.

5.4 Phase II: Ambulatory exercise training phase

Goals:

- Reinforce cardiac risk factor modification
- Provide education and support to patient and family
- Promote continuing adherence to lifestyle recommendations
- Structured exercise training with continual educational and psychological support and advice on risk factors
- Should take a menu-based approach and be individually tailored.
- Typically lasts at least 12 weeks with patients exercising at least 2-3 days per week.
- Exercise class will consist of a warm-up, exercise class, cool down – may also include resistance training with active recovery stations where appropriate.
- Target exercise Intensity of 50-85% MPR, which involves graded supervised exercises-both aerobic and resistance training
- Home-based unsupervised exercises of reduced intensity.

5.5 Phase III: Maintenance

Goals:

- Facilitate long term maintenance of lifestyle changes, monitoring risk factor changes and secondary prevention.

5.6 What are the benefits of Cardiac Rehabilitation?

5.6.1 Mortality reduction:

A 2011 Cochrane review and meta-analysis of 47 randomised controlled trials that included 10,794 patients showed that cardiac rehabilitation reduced overall mortality (relative risk 0.87 (95% confidence interval 0.75 to 0.99), absolute risk reduction (ARR) 3.2%, number needed to treat (NNT) 32) and cardiovascular mortality (relative risk 0.74 (0.63 to 0.87), ARR 1.6%, NNT 63), although this benefit was limited to studies with a follow-up of greater than 12 months(3).

Improvement in cardio-respiratory fitness in 12weeks was associated with decreased mortality overall, with a 13% point reduction (hazard ratio [HR], 0.87; 95%CI, 0.79-0.96) in mortality with each MET increase (P<.001). (4). The higher baseline fitness predicted lower mortality. Improvement in fitness during a CR program and improvements that persisted at 1 year were also associated with decreased mortality, most strongly in patients who start with low fitness.

The 2016 Updated Cochrane Systematic Review & Meta-analysis on Exercise for Coronary Artery Disease of 63 studies with 14,486 participants with a median follow-up of 12 months, CR led to a reduction in cardiovascular mortality by 26% and the risk of hospital admissions by 18%(5). This demonstrated an absolute risk reduction in cardiovascular mortality from 10.4% to 7.6% (NNT 37) for patients after myocardial infarction and revascularization who received cardiac rehabilitation compared with those who did not.

5.6.2 Reduced Hospital admissions

Anderson et al also demonstrated that CR reduced risk of hospital admission from 30.7% to 26.1%, NNT 22.(5). In another Cochrane review of 4740 patients with heart failure, exercise-based cardiac rehabilitation reduced the risk of overall hospitalisation (relative risk 0.75 (0.62 to 0.92), ARR 7.1%, NNT 15) and hospitalisation for heart failure (relative risk 0.61 (0.46 to 0.80), ARR 5.8%, NNT 18). (6)

5.6.3 Improvement in psychological well-being and quality of life

Several studies have reported improvement in psychological stress in patients with coronary heart disease who have attended cardiac rehabilitation. A meta-analysis of 23 randomised controlled trials of 3180 patients with coronary heart disease, that evaluated the impact of adding psychosocial interventions to standard exercise-based cardiac rehabilitation reported a greater reduction in psychological distress (effect size 0.34) and improvements in systolic blood pressure and serum cholesterol (effect sizes −0.24 and −1.54 respectively).(7).

A Cochrane review of exercise-based cardiac rehabilitation for heart failure reported a clinically important improvement in the Minnesota Living with Heart Failure questionnaire (mean difference 5.8 points (95% confidence interval 2.4 to 9.2), P=0.0007) in the 13 randomised controlled trials that used this validated quality of life measure. (6)

5.6.4 Improvements in Functional capacity and Cardio-Pulmonary function

Significant improvements in functional capacity (VO2max, METS achieved, and 6MWT) and cardio-pulmonary function (VT, VO2max), Increased lean mass and improved autonomic functions with CR have been documented in multiple trials. These often translate into improved quality of life(8–11). Long-term (over 10 years) survival among patients with stable CAD, when stratified based on their baseline fitness levels (as low: <5METs, moderate: 5-8METs and high: >8METs) was shown to be best among patients with a high baseline fitness level. Greater survival benefit is seen associated with a modest increase in physical activity in sedentary persons and the amount of mortality reduction decrease progressively at higher levels of exercise.

5.6.5 Improvement in Cardio-vascular risk Profile

Cardiac rehabilitation programs provide education and counselling services to help increase your physical fitness, reduce cardiac symptoms and lower your risk of future heart problems, including a heart attack. Research shows that regular physical activity can strengthen your heart and body, improve your energy, boost your mood, and reduce the risk of heart problems. (12)

5.7 Who will benefit from Cardiac rehabilitation?

According to multiple international scientific societies, the beneficiaries of CR include the following:

1. Patients with ACS (Acute Coronary Syndrome) – STEMI, NSTEMI and Unstable Angina and all patients undergoing revascularization/ reperfusion with Coronary Artery Bypass Graft (CABG) or Percutaneous Coronary Angioplasty (PCI).
2. Patients with Chronic Heart Failure
3. Patients with a Heart transplant and Ventricular Assist device
4. Patients with ICD or CRT inserted for reasons other than for heart failure
5. Patients following heart valve surgeries
6. Patients with a confirmed diagnosis of chronic stable angina.

In some intervention group, separate programs are provided for people with different diagnoses; however, in many instances, the approach adopted will address the differing needs of these groups. It may also be appropriate for patients awaiting cardiac investigation or intervention to attend inpatient or outpatient cardiac rehabilitation programs.

People with other presenting problems, such as Type 2 diabetes or multiple cardiac risk factors, may also participate in cardiac rehabilitation as many elements have broad relevance; however, these recommendations are based around the needs of the above-mentioned core group

5.8 What are the risks and contra-indications for exercise-based CR?

ESC criteria of risk stratification for cardiac events during exercise training, post-MI(13):

	Low event risk	Moderate risk	High risk
In-hospital course	Without complications	Angina	Re-infarction Clinical CHF
Functional Capacity	> 7 METs	5 – 7 METs	< 5 METs
Evidence of Ischemia	Nil	Reversible ischemia by the stress test	>2mm ST changes with EST Hypotensive response to EST
LVEF	> 50%	35-49%	< 35%
Ventricular Arrhythmias	Nil	Nil Severe	Malignant Ventricular arrhythmias

Absolute and Relative contraindications for cardiopulmonary exercise testing

Adopted from ATS/ACCP Statement on Cardiopulmonary Exericse Testing (14)

Absolute Contraindications for cardiopulmonary exercise testing
Acute myocardial infarction (3-5 days)
Unstable Angina
Uncontrolled arrhythmias causing symptoms or haemodynamic compromise
Syncope
Active endocarditis
Active myocarditis or pericarditis
Symptomatic severe aortic stenosis
Uncontrolled heart failure
Acute Pulmonary embolus or pulmonary infarction
Thrombosis of lower extremities
Suspected dissecting aneurysm
Uncontrolled asthma
Pulmonary oedema
Room air desaturation at rest $\leq 85\%$
Respiratory Failure
Acute non-cardiopulmonary disorder that may affect exercise performance or be aggravated by exercise (i.e., infection, renal failure, thyrotoxicosis)
Mental impairment leading to inability to cooperate

Relative Contraindications for cardiopulmonary exercise testing
Left main coronary stenosis or its equivalent
Moderate stenotic valvular heart disease
Sever untreated arterial hypertension at rest at rest or haemodynamic compromise (>200 mm Hg systolic, >120 mm Hg diastolic)
Tachyarrhythmias or bradyarrhythmia's
High-degree atrioventricular block
Hypertrophic cardiomyopathy
Significant pulmonary hypertension
Advanced or complicated pregnancy
Electrolyte abnormalities
Orthopedic impairment that compromises exercise performance

5.9 What are the Adverse events (AE) related to exercise testing?

- Incidence (overall) : 7.25events /100,000 tests
- Life-threatening AE: 0.64/100,000 tests
- AMI/ Cardiac arrest: 1 /160,000 to 1/250,000 tests

5.10 What are the barriers to CR especially with respect to India?

Although an essential component in the prevention & management of cardiovascular diseases, CR is still under-utilized worldwide. CR is available in 68.0% of high-income, 28.2% of middle-income, and 8.3% of low-income countries(15)

In India, CR is in a nascent stage. Availability of structured exercise-based CR services is minimal. There is a scarcity of data on the proportion of eligible participants receiving CR and various factors influencing CR participation. Potential barriers to CR can be classified as health-care system barriers (including infrastructure and staffing), health-care professionals-related barriers, and patient-related barriers. (16)

5.11 How to address these barriers?

5.11.1 Structured exercise program

A structured exercise programme has been identified as being central to the success of cardiac rehabilitation. Aerobic endurance training is the foundation for the exercise component of cardiac rehabilitation. Exercise-based cardiac rehabilitation is an effective and safe therapy to be used in the management of clinically stable patients following myocardial infarction or percutaneous coronary intervention or who have heart failure. (17)

5.11.2 Aerobic Interval Training (AIT):

Interval training is a well-known method for improving fitness. Technically, it is defined as high-intensity intermittent exercise. In an interval session, high-intensity periods of work are interspersed with rest intervals.

In this way athletes can cover more distance at a high intensity than they could if they worked continuously. Because interval training is intense, it is a great method for improving both aerobic and anaerobic fitness.

Interval-training sessions can be different in composition, as there are three variables that can be altered: the intensity (speed), the work period and the rest period

However, without accurate analysis of the aerobic and anaerobic energy demands of each session, it is impossible to say which session is the more effective, or whether the sessions place the same demands on the energy systems.

With this is mind, Izumi Tabata and his colleagues at the Japanese Institute of Fitness and Sport designed an experiment to measure how two different types of interval training sessions taxed the aerobic and anaerobic energy systems (18)

Mitochondrial responses to interval training

Skeletal muscle mitochondrial density regulates substrate metabolism during submaximal exercise, with increased mitochondrial content promoting a greater reliance on fat oxidation and a proportional decrease in carbohydrate. As a result, exercise training lessens glycogen degradation and lactate production at a given intensity, while increasing the lactate threshold and allowing individuals to exercise for longer durations and at greater percentages of their V˙O2max .Thus, given its central role in exercise performance, there is considerable interest in the factors mediating exercise-induced mitochondrial adaptations(19)

The role of skeletal muscle recruitment pattern and fiber type

Skeletal muscle recruitment occurs in proportion to exercise intensity, implying that higher intensities of exercise could elicit greater responses in type II fibers relative to

lower intensities of exercise. Mitochondrial content would be greater in type II fibers following HIIT as compared to MCT. (20)

Interval training and skeletal muscle capillary density

Skeletal muscle capillarization requires weeks to months to manifest in response to exercise training and changes in capillary density appear to be blunted at higher exercise intensities. Low-volume SIT induced similar or greater increases in the expression of several angiogenesis relative to MCT, including greater vascular endothelial growth factor (VEGF) expression. In the one comparison of work-matched HIIT and MCT skeletal muscle capillarization increases were greatest following MCT.(21)

Both the high-intensity activity and lower intense activity can be measured as a percentage of Maximum Heart Rate (MHR), Volume of maximum oxygen consumption (VO2max) or an individual's Rate of perceived exertion (RPE). (22)**Advantages**

- AIT can be effective for improving aerobic capacity and/or calorie burning in less time when compared to high-volume, steady-state training.
- The higher-intensity work intervals of HIIT can be based on an individual's RPE, allowing that individual to start exercising at relatively low intensity (as measured objectively) and progress from that initial starting point.
- Interval training may be an effective strategy for individuals who become easily distracted or bored during longer exercise sessions.
- Can improve the efficiency of type II muscle fibres to produce energy via anaerobic glycolysis, resulting in greater metabolic efficiency.

- Exercising above the lactate threshold can help stimulate the production of muscle-building, fat-burning hormones such as testosterone, growth hormone and insulin-like growth factor.
- Increases the effect of EPOC (excess post-exercise oxygen consumption), helping to burn calories after the exercise session is completed.

Disadvantages

- AIT exercise increases mechanical damage on muscle tissue, which could increase soreness and the perception of exercise as “painful” in deconditioned individuals.
- Anaerobic metabolism results in an accumulation of metabolic stress that limits a muscle’s ability to function.
- The high mechanical stresses of AIT can increase the risk of a muscle strain.
- The higher exercise intensities required to improve aerobic conditioning with AIT may be uncomfortable or painful for some people.

5.11.3 Moderate Continuous Training (MCT):

It involves maintenance of consistent speed, level of intensity and work rate during an exercise session.

Advantages

Exercising below the ventilatory threshold for an extended period of time puts less physical stress on the cardiorespiratory system and can be an effective way to prepare for an endurance event.

- It is an established and proven method for improving cardiorespiratory fitness and enhancing aerobic capacity.
- Increases mitochondrial density in type I (slow twitch) muscle fibres, which can improve aerobic metabolism.
- Increases cardiac efficiency; specifically, elevating stroke volume and cardiac output at a lower heart rate.
- Enhances ability to use fat as an efficient fuel source, which reserves muscle glycogen to be used for higher-intensity exercise.
- Steady-state training to improve aerobic efficiency generates less metabolic waste and cellular damage than HIIT workouts.

Disadvantages

- If the goal is weight loss, steady-state training may require extended periods of training time to achieve the desired level of caloric expenditure.
- Using steady-state training to improve aerobic capacity may require lengthy exercise sessions, which can be a challenge for a busy lifestyle.
- Extended periods of exercise can increase the risk of repetitive stress injuries.
- Certain individuals may find it difficult to maintain the focus necessary to train at a constant work rate for an extended period.

5.11.4 Resistance Training (RT)

Supervised resistance training (RT) enhances muscular strength and endurance, functional capacity and independence, and quality of life while reducing disability in persons with and without cardiovascular disease (CVD). These benefits have made RT an accepted component of programs for health and fitness

The potential benefits, not only to cardiovascular health but also to weight management and the prevention of disability and falls, are becoming more widely appreciated. For persons at low risk for cardiac events, extensive cardiovascular screening is probably not necessary, although a graded approach is recommended. For persons at moderate to high risk of such events, RT can be safely undertaken with proper preparation, guidance, and surveillance.

Because long-term compliance remains a challenge for adult fitness and exercise-based cardiac rehabilitation programs, the incorporation of RT can provide variety in the training regimen and can increase the potential for maintenance of interest and improved compliance. However, given the extensive evidence of the benefits of aerobic exercise training on the modulation of cardiovascular risk factors, RT should be viewed as a complement to rather than a replacement for aerobic exercise.(23)

Recommendations from the American Association of Cardiovascular and Pulmonary Rehabilitation AACVPR 2013(23)

- Minimum of 5 weeks after the date of MI or cardiac surgery, including 4 weeks of consistent participation in a supervised CR endurance training program

- Minimum of 3 weeks following transcatheter procedures (PCI, other), including 2 weeks of consistent

Resistance training within a cardiac rehabilitation system can be a healthy and effective alternative to conventional aerobic training. Most cardiac patients that lack the muscle strength, cardiovascular and/or muscular endurance and/or self-confidence necessary to carry out daily activities involving regular muscle contractions with equal or total effort.

Therefore, three areas in which resistance training can enhance the rehabilitation process are (a) improvements in absolute strength, (b) increased cardiovascular endurance, and (c) increased self-confidence in carrying out professional and recreational activities where strength is required(24)

Many daily tasks involve isodynamic or static contractions of the muscles, improving strength after a heart event is imperative for the heart patient. Because isodynamic and static activities generate predominantly a pressure response, it would seem logical to use specific training to strengthen the muscle system. This could then reduce the pressure response due to the reduced percentage of maximum voluntary contraction after training. This could then reduce the pressure response due to the reduced percentage of maximum voluntary contraction after training.

For the single-arm curl, single-leg press, and single-knee extension, McCartney et al(25). experienced an increase of 43, 21, and 24 percent respectively. The results of performing repeats to failure using the initial 1RM were more impressive. Combined group subjects performed 14, compared to only 4 control group repetitions.

These data indicate that resistance training, employing up to 80 percent of 1RM, can induce substantial strength gains without adverse consequences for low-risk cardiac patients.

An individual who has experienced a heart event may sometimes be limited by his / her mental attitudes and beliefs regarding the performance of certain tasks, not by his / her physical abilities.

People involved in cardiac rehabilitation tend to show improved self-esteem and quality of life. Resistance training can play a valuable role in strengthening and influencing the self-perception and self-efficacy of a person in the performance of daily tasks requiring low to medium strength.(26)

Nevertheless, the increased self-efficacy is exercise-specific, indicating that it is necessary to include a varied approach in the recovery activities.

5.11.5 Home-based vs Centre based CR

In several Western Studies and Cochrane systematic review and meta-analysis 2010, home and centre-based forms of cardiac rehabilitation seem to be equally effective in improving clinical and health-related quality of life outcomes in patients with a low risk of further events after myocardial infarction or revascularization. However, we do not have any Indian studies to compare the efficacy between Home and centre-based cardiac rehabilitation. (27–29)

Using Home-based CR (HBCR), either alone or in combination with Center-based CR (CBCR) is a possible alternative that can enhance CR delivery to eligible patients.

HBCR has been incorporated into several countries ' healthcare systems, including Australia, Canada, and the UK. The British Heart Foundation recently reported that > 50% of eligible patients in the United Kingdom now participate in CR following a heart event or procedure.

HBCR has the potential to expand the scope and depth of patient education, counseling and monitoring options as HBCR services can potentially be used 24 hours a day, 7 days a week, while most CBCR programs are usually limited to 3 to 4 hours of weekly in-person contact between patients and employees.

Although home-based exercise learning is widely recommended to their clients by CBCR staff on days when they are not physically present at the CBCR clinic, "stand-alone" HBCR programs are still in their infancy.

Considering that severe cardiovascular events are uncommon even in CBCR studies, including a mix of patients at lower and higher risk, HBCR studies are currently underpowered to assess the risk of severe cardiovascular events, particularly in patients at higher risk.

Because of this limitation, in the studies we reviewed of HBCR versus CBCR, the safety results are comparable, at least in the low to moderate-risk patients included in most studies. For earlier studies, studies involving higher-intensity training, and those involving older patients, a focus on health was mostly apparent.

At a time when CVD patients are more likely to be older and frail, have more comorbidities, and are at higher cardiovascular risk, HBCR's clinical safety and efficacy assumptions for these patients deserve more scrutiny.(28,29)

Advantages and Disadvantages of HBCR compared with CBCR	
Advantages	Disadvantages
Reduced Enrollment delays	Lack of reimbursement
Expanded fitness capacity	Less intense exercise training
Individually tailored programs	Less social support
Flexible, convenient scheduling	Less patient accountability
Minimal travel barriers	Lack of published standards
Greater privacy while receiving CR services	Less face to face monitoring and communication
Integration with regular home routine	Safety concerns for patients a higher risk

Adopted from Scientific Statement From the American Association of Cardiovascular and Pulmonary Rehabilitation, the American Heart Association, and the American College of Cardiology

5.12 Primary Outcome measures of the study:

5.12.1 Functional capacity as assessed with METS, Vo2 max, 6MWT:

Functional capacity can be measured directly by determining $\dot{V}O_2$max using cardio-pulmonary testing or estimated from the highest treadmill or cycle work rate achieved. In these settings, $\dot{V}O_2$max can be estimated from published nomograms. It must be recognized, however, that there may be a sizeable discrepancy between estimated and measured $\dot{V}O_2$max because of the use of handrail support, differences in gait, different degrees of familiarity with treadmill exercise, and differences between the populations being tested and that from which the formula for estimating $\dot{V}O_2$max was derived. For these reasons, when an accurate and reproducible objective assessment of aerobic capacity is needed, $\dot{V}O_2$max should be measured directly.

The selection of an appropriate protocol for assessing functional capacity is of critical importance. When aerobic capacity is to be estimated from exercise time or peak work rate, protocols with large stage-to-stage increments in energy requirements should be avoided because of their weaker relationship between oxygen uptake and work rate. The Balke and Naughton protocols, which involve only modest increases in treadmill elevation at a constant speed, are preferable for this purpose.

Regardless of the specific protocol chosen, the protocol should be tailored to the individual to yield a fatigue-limited exercise duration of ≈10 minutes. Shorter durations may produce a nonlinear relationship between $\dot{V}O_2$ and work rate, whereas durations

>12 minutes may cause subjects to terminate exercise because of muscle fatigue or orthopaedic factors.

5.12.2 METS by Treadmill testing:

Among men with and without cardiovascular disease who were referred for treadmill exercise testing, peak exercise capacity measured in metabolic equivalents (METs) was the strongest predictor of the risk of death, during an average of 6.2 years follow-up. For each 1-MET increase in exercise capacity, there was a 12 per cent improvement in survival. (30). Similarly, exercise capacity was shown to be an independent predictor of death in asymptomatic women. (31)

In the Research on Instability in Coronary Artery Disease study, the major predictors of 1-year infarction free survival in 740 men with unstable angina or non–Q-wave myocardial infarction who underwent pre-discharge cycle ergometer exercise testing were the number of leads with ischemic ST-segment depression and peak workload attained(32)

In a total of over 15,000 patients from 39 countries with stable CHD, more physical activity was associated with lower mortality. The largest benefits occurred between sedentary patient groups and between those with the highest mortality risk(33)

TMT Bruce Protocol

A trained cardio technician performs and supervises TMT. ECG electrodes are linked to the body attached to the ECG system which tracks the heart's electrical activity throughout the operation. Resting ECG, heart rate and blood pressure are collected before the exercise routine is initiated.

When the baseline recordings are complete, the patient begins to walk slowly (less than 2 miles an hour) on the treadmill. Bruce's protocol is divided into successive 3-minute stages, each requiring the patient to walk more quickly and steeper. The test protocol could be adjusted to the tolerance of a patient for a duration of exercise of 6 to 12 minutes.

For those who cannot exercise regularly, there is a revised Bruce protocol which introduces two lower stages of workload to the end of the regular Bruce protocol, both of which require less effort than Stage 1. Upon reaching the target, walk slowly for a few minutes to cool down and then stand or sit still for another 15 minutes or so while your heart returns to its state of rest.

Before starting the exercise portion of the test, the baseline ECG should be evaluated closely. The rest ECG is usually obtained both standing and standing, as the position of the patient can influence the QRS and T axes of the wave.

During the exercise test, data should be obtained at the end of each stage on heart rate, blood pressure and ECG changes and an abnormality should be detected with cardiac monitoring at any time. With each exercise phase, heart rate and systolic blood pressure must increase until a plateau is reached. Patients should be asked about any symptoms

during exercise. During the recovery period, all patients should be closely monitored until the heart rate, and ECG is back to baseline as arrhythmias and changes in the ECG may still occur.

At the onset of mild symptoms, exercise should not be interrupted if there are no known ECG irregularities and the patient is hemodynamically stable. Test termination signs include when the patient requests to stop due to severe symptoms (e.g. chest pain, shortness of breath and fatigue), serious exercise-induced hypotension or hypertension, horizontal or downward ST depression or new bundle branch block, AV block, ventricular arrhythmia, if patients achieve their maximal heart rate or all stages have been completed.

A report should be included at the end of the test. This report should outline the basic ECG interpretation, baseline heart rate and blood pressure, ECG changes during exercise including the presence and onset of arrhythmia / ectopia, maximum heart rate and blood pressure during exercise, estimated MET exercise capacity, duration of exercise and completed stage and the reason for terminating the test.

A normal test is when there is an appropriate increase in patient blood pressure and heart rate for graded exercise. During screening, there should be no possible ECG shifts of ischemia and no arrhythmias. There is a strong prognostic indicator that blood pressure does not increase or decrease with signs of ischemia.

Before completing stage 2 of the Bruce protocol a ST depression that persist in recovery for more than 5 minutes, angina or significant ST depression (greater than 2 mm) suggest severe ischemia and high risk of coronary events. If there is a limiting factor

such as heart rate, exercise analysis will be either positive, negative, deceptive or uninterpretable.(34)

Stage	Minutes	% Grade	Kmph	Mph	METS
1	3	10	2.7	1.7	5
2	6	12	2.5	2.5	7
3	9	14	5.4	3.4	10
4	12	16	6.7	4.2	13
5	15	18	8.0	5.0	15
6	18	20	20	5.5	18
7	21	22	22	6.0	20

Stages of Bruce Protocol

5.12.3 6MWT (6-minute walk test)

Assessment of exercise capacity by means of the 6MWT is most frequently used in pulmonary and cardiac diseases. This measure the distance a person can quickly walk on a flat, hard surface in 6 minutes (the 6MWD). The 6MWT requires a 30-meter (100 ft) corridor, stopwatch, two small cones to mark the turnover points, one chair that can be easily moved along the walking course to support the patient, an available source of oxygen, a sphygmomanometer or other validated blood pressure measuring devices, and a defibrillator.

The length of the hallway should be marked every 3 meters with a cone, and the starting line should be marked on the floor using brightly coloured tape. In the case of repeating

the test, it is important that it should be performed at the same time of the day and without any "warmup." The patient should rest seated on a chair located near the starting line for at least 10 minutes before the test starts. (35)

Indications and limitations

The best reason for the 6MWT is to evaluate the reaction in moderate to severe heart and lung disease patients to medical interventions.

The 6MWT does not determine peak oxygen intake, diagnose the cause of exertional dyspnea, or assess the causes or mechanisms of limiting exercise. The information provided by a 6MWT should be considered complementary to, and not a replacement for, cardiopulmonary exercise testing

Despite the difference between these two functional tests, there have been reports of some good correlations between them. For example, patients with end-stage lung diseases have been reported to have a significant correlation between 6MWD and peak oxygen intake

In some clinical situations, the 6MWT provides information that may be a better index of the patient's ability to perform daily activities than peak oxygen absorption; for example, 6MWD is better correlated with formal quality of life measures.

Absolute 6MWT contraindications include unstable angina in the preceding month and myocardial infarction in the preceding month.

Relative contraindications include a more than 120 resting heart rate, a more than 180 mm Hg systolic blood pressure, and a higher than 100 mm Hg diastolic blood pressure.

Stable exertional angina is not an absolute contraindication for a 6MWT, but patients with these symptoms should take the test after using their antianginal medication, and nitrate rescue medication should be readily available

5.12.4 Vo2 Max

Peak VO2 is a strong indicator of heart failure severity and is an important factor in the timing of heart transplantation, and the 6MWT distance is strongly correlated with peak VO2 in HF patients with reported correlation coefficient in the range from r = 0.56 to r = 0.88. The correlation between 6MWT and peak VO2 in patients with heart failure is stronger in patients with low 6MWT and low peak VO2; then, 6MWT becomes less predictive as peak VO2 value becomes higher. The 6MWT is reliable, valid, and predictive for patients with heart failure who do not walk greater than 490 meters.(36) } However, other studies suggest that VO2 peak is a better predictor of survival, particularly over longer follow-up periods.

In 133 elderly patients undergoing cardiac surgery, Afilalo et al. reported that slow gait speed defined as the time taken to walk 5 meters in >6 seconds was associated with a higher risk of in-hospital complications from surgery. (37)

Indications for exercise Termination

Indications for exercise Termination
Chest pain suggestive of ischemia
Ischemic ECG changes
Complex ectopy
Second- or third-degree heart block
Fall in systolic pressure >20mm Hg from the highest value during the test
Hypertension (>250mm Hg systolic: >120 mmHg diastolic)
Severe desaturation: SPo2<80% when accompanied by symptoms and signs of severe hypoxemia
Sudden pallor
Loss of coordination
Dizziness or faintness
Signs of respiratory failure
Mental confusion

Adopted from ATS/ACCP Statement on Cardiopulmonary Exericse Testing(14)

Cardiopulmonary Exercise Test Parameters Used to Differentiate Cardiac And Pulmonary Causes Of Exertional Dyspnoea

	Cardiac	pulmonary
Vo2 Max	Achieved but low	Not achieved
Peak Vo2	Reduced	Reduced
VT	Yes, But low	Rarely achieved
VEmax	<50% True MVV	>50% True MVV
SaO2	Normal	May drop to <90%
CO	Normal or low	Normal
VT - ventilatory threshold; MVV-maximal voluntary ventilation, SaO2- arterial oxygen saturation		

5.12.5 LV Remodelling

Reverse LV remodelling as assessed with echocardiographic parameters - ESV, LVEF, LV-GLS, LV septal e/e'

Following an MI, changes occurring in LV geometry are well documented. LV remodelling historically refers to the maladaptive change in cardiac geometry that occurs following an MI. The characteristic feature is LV cavity enlargement. A chamber enlargement and poor LV function lead to elevated wall stress, increasingly spherical

geometry and development of functional mitral regurgitation, all of which contribute to further remodelling. Re-modelling is defined as the changes in LV end-diastolic volume (LVEDV) and/or end-systolic volume (LVESV) between discharge and late follow-up measurements. Adverse remodelling refers to a clinically significant increase in LVEDV whereas reverse remodelling is defined as a clinically significant decrease in LVESV or improvement in LV ejection fraction (LVEF).

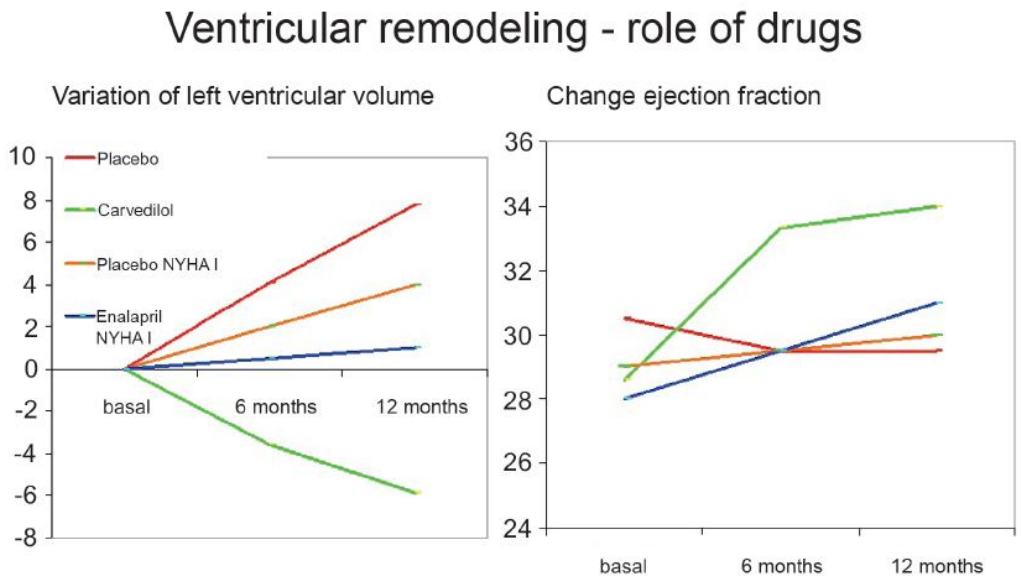
Adverse LV remodelling is often described as an increase in LVEDV and/or LVESV by 15 to 20%. Reverse LV remodelling is described with myocardial recovery. This is often assessed by improvement in LVEF greater than 5% or a decrease in LVESV greater than 15%. Despite the high success rate of percutaneous coronary revascularization in acute MIs, adverse LV remodelling occurs in one-third of patients (12 - 44%) with a rate of LV recovery ranging from 12 - 54%.

In a Systematic Review & Meta-analysis, Huttin et al reported an association between pre-discharge Global Longitudinal Strain (GLS) and degree of LV remodelling. They described that the most accurate cut-off value of GLS to predict adverse LV remodelling and reverse remodelling ranged from -12.8% to -10.2% and from -13.7% to -9.5%, respectively. In the multivariate-adjusted analysis, GLS provided significant incremental value over clinical and conventional echocardiographic variables in predicting global LV function improvement or LV remodelling. (38)

Evidence on the importance of reverse LV remodelling in HF prognosis is steadily growing. Patients who present regression of ventricular dilation or increased ejection fraction after treatment have a better quality of life. At follow-up, Cioffi et al.

demonstrated that patients with reverse cardiac remodelling had lower mortality (3%) compared with those who did not present reversal (22%)(39). Hoshikawa et al. observed that prognosis is related to the reversal of cardiac dilation. They divided their patients into three groups: those with full reverse cardiac remodelling, with LV diameter < 55 mm and Delta D fraction > 25%; those with partial reversal; and those who did not present reversal. They observed that those with no reversal of cardiac dilation died during follow-up, which lasted an average of 5 years. All patients who had some reversal survived. In that study population, all patients were treated with neurohormonal blockers; 78% showed a reversal of cardiac dilatation and, of these, 57% showed a complete reversal. (40)

Cardiac dilation is not reversed in all patients with HF and ventricular dysfunction. In patients with lesser involvement, reversal is not generally observed; it is more frequently identified in intervention group of moderate to intense involvement, with greater magnitude in the former(41). Studies have shown a reversal of cardiac dilation in approximately 30%–60% of the intervention group treated with neurohormonal blockers. Adrenergic activity actually plays an important role in ventricular remodelling, greater than that of the renin-angiotensin system, at least in the most symptomatic forms of the disease. (42) ACE inhibitors are shown to prevent cardiac dilation and beta-blockers reverse it. (43)



McGregor et al demonstrated that 10weeks of cardiac rehabilitation exercise training improved functional capacity and resulted in reverse LV remodelling in a population of post-MI patients with preserved LVEF.**(44)**. Exercise training has beneficial effects on LV remodelling in clinically stable post-MI patients, with greatest benefits occurring when training starts earlier following MI (from one week) and lasts longer than 3 months. (36) Aerobic exercise training, especially long-term duration (≥6 months) reverses left ventricular remodelling in clinically stable patients with heart failure. Strength training (alone or with aerobic training) did not improve or worsen ventricular remodelling. (7)

Right Ventricle tricuspid annular plane systolic excursion (TAPSE):

Right ventricular (RV) function is an important predictor of outcome in several cardiovascular diseases and a precise evaluation of RV function is therefore necessary. Nevertheless, the right ventricle's peculiar geometry raises volume and therefore ejection fraction assessments in both normal and disease states by two-dimensional (2D) echocardiography.

Due to the lack of any widely accepted 2D echocardiographic methods for assessing RV systolic function (RVSF), an objective assessment of the RV function remains difficult in clinical practice.

RV ejection fraction (RVEF) typical echocardiographic surrogates include tricuspid annular systolic plane excursion (TAPSE) and fractional area shift (FAC). TAPSE is a one-dimensional RVSF measure and assumes that the displacement of basal and adjacent RV segments is the whole RV feature.(45)

5.12.6 Heart Rate Recovery @ 1minute

HRR, an index of vagal activity, is an independent predictor of cardiovascular events and mortality, and patients after AMI usually present a delayed HRR. Over-activation of the sympathetic system is harmful to patients' ventricular remodelling, clinical symptoms and long-term survival.

The value for the recovery of heart rate is defined as the decrease in the heart rate from peak exercise to one minute after the cessation of exercise. Reduction of 12 beats per minute or less from the heart rate at peak exercise is considered abnormal. A delayed

decrease in the heart rate during the first minute after graded exercise, which may be a reflection of decreased vagal activity, is a powerful predictor of overall mortality, independent of workload, the presence or absence of myocardial perfusion defects, and changes in heart rate during exercise. (46)

Heart rate recovery (HRR) is characterized as the speed at which the heart rate decreases within minutes of physical exercise cessation and represents the complex balance and coordination between parasympathetic reactivation and sympathetic withdrawal.(46)

As a simple and non-invasive assessment of autonomous nervous system function which can indicate one's ability to adapt to exercise stimuli, HRR has received considerable interest and is commonly used as a tool for tracking improvements in physical fitness and training status

There has been a wide range of epidemiological evidence in recent years that HRR may also be a possible prognostic marker for predicting health outcomes like cardiovascular disease (CVD), as it has been proposed that autonomic dysfunction as attenuated HRR is a precursor to hyperglycemia as well as a predictor of cardiovascular dysfunction.(47)It is biologically plausible that a decreased HRR may result in a continuum of poor health outcomes as shown in our research, although the exact underlying mechanisms remain unclear.

1. First, evidence suggests a clear and specific dose-response correlation between HRR and cardiorespiratory health, whereas the latter has been shown to be closely linked to the risk of cardiovascular events and all-cause mortality.
2. Secondly, it is well recognized that the autonomous nervous system is essential in maintaining glycemic homeostasis, where parasympathetic fibers stimulate

the β cells to release insulin in response to high levels of glucose, and sympathetic activation inhibits insulin secretion. Dysfunction of the autonomic nervous system as a result of attenuated HRR would result in reduced insulin secretion but increased levels of glucose, leading to the development of diabetes mellitus and disorders such as CVD through multiple mechanisms including glucose toxicity, inflammation and endothelial dysfunction.(47)

3. Third, a recent cross-sectional study by Kuo et al found that chronic inflammation and insulin resistance were inversely related to HRR, while both factors were CVD characteristics.(48)
4. Finally, since HRR may reflect the function of the parasympathetic nervous system and given that increased parasympathetic tone has antiarrhythmic effects, it is conceivable that attenuated HRR would predict death due to the potential increased risk of cardiac arrhythmias(49)

5.13 What are the possible mechanisms of reverse LV Remodelling?

From pharmacological trials, we now know that suppression of neurohormonal and autonomic responses can minimize LV remodelling following MI. Exercise training in heart failure is also shown to cause attenuation of the negative neurohormonal and autonomic responses associated with LV remodelling. Apart from these, the vascular adaptation to exercise help normalize LV afterload. (50)

In both humans and animals, heart remodeling also represents a maladaptation for response to infection or underlying pathology. The expansion of the ventricular cavities or increase in the thickness of the myocardial wall occurs in response to increased volume or wall stress. Thus, heart disease-related altered hemodynamics, such as valvular regurgitation or aortic stenosis, result in adverse cardiac pathological remodeling. However, physiological changes in the hemodynamic loading of the heart during exercise are also inevitable The heart can feel an increased volume load, an increased "stress" afterload, or indeed a combination of both, depending on the specific exercise stimulus. Therefore, when exercise is performed frequently in a structured manner over a prolonged period, like that recommended for competitive athletes, there are strong reasons for cardiovascular adaptation and remodelling.

Athlete's Heart:

Cardiac remodeling is a well-described phenomenon in humans in response to physical training. As early as the 1890s, doctors in Sweden and the USA showed increased cardiac dimensions in elite cross-country skiers and rowers, respectively, using auscultation and percussion.(51,52). The first findings of cardiovascular bradycardia in Boston Marathon runners preceded these data.(53) Subsequently, many studies have characterized the structural and functional adaptations observed in the human heart in response to athletic training with improved imaging.

The sport has been guided by a dichotomous interpretation of the heart of the athlete since the mid-1970s. Specifically, it was proposed that endurance athletes pose with

cardiac adaptations caused by increased "size" load, while power-based athletes have a cardiac phenotype formed by a lower "stress" load.

Simplistically, endurance athletes have broad, eccentrically remodeled hearts - large ventricular volumes, moderate wall thickening, and low relative wall thickness - with reduced heart rate, whereas power athletes with concentrated remodeling - thick ventricular walls, relatively small ventricular volumes, and high relative wall thickness with limited heart rate change. In systemic blood pressure, the latter is postulated to be caused by peaks, and hence ventricular wall stress associated with repeated strength / power-based activities. Morganroth initially made this dichotomous distinction between strength and power athletes and was later called the "Morganroth hypothesis."(54). This view has been widely accepted in the literature on sports cardiology until recently. While this hypothesis is attractive from a physiological basis, however, in response to athletic training, it is probably an over-simplistic representation of cardiac remodeling.

Acute Exercise and Cardiac Loading

Increased metabolic and thermoregulatory demand is associated with aerobic exercise. Such conflicting demands must be met by improved blood supply to both the working muscle and the capillary beds responsible for heat exchange for exercise to proceed for any time beyond a few seconds. This apparent need for increased blood flow during exercise explains the close relationship between cardiac and the quantity of oxygen absorbed per minute(55)

In humans, heart rate and stroke volume increase in dynamic (isotonic) aerobic exercise, along with a modest decrease in overall systemic vascular resistance; the net result is a

significant increase in cardiac output. In contrast, a more modest increase in cardiac output is observed during resistance or static (isometric) exercise, driven primarily by an increase in HR, but also accompanied by a more pronounced increase in systemic blood pressure than during dynamic aerobic exercise. Therefore, the heart-imposed hemodynamic load depends on the frequency, length, and modality of the exercise. Importantly, exercise is rarely either dynamic or static in isolation, but most sports fall somewhere along a continuum involving both elements.

To better characterize the relative load of individual sports, Mitchell and colleagues proposed an extended matrix, which provides a much better representation of the cardiovascular "mixed" load to which athletes ' hearts are exposed. Despite this, in the context of either an exercise-induced pressure or volume stimulus, much of the available literature on cardiac remodeling in human athletes due to exercise was presented.

Right ventricle remodelling

To date, most work has focused on the LV to examine the heart of the athlete. This is probably a consequence of the important role that the LV plays in generating the cardiac output needed to meet the exercise demands but is also likely to be related to the relative ease associated with the left side of the heart imaging. Nevertheless, a growing body of work has been completed to explore the capacity of the right ventricle, atria, and aorta for remodeling in response to human athlete practice. Since exercise requires an increase in the volume of the stroke in both the left and right ventricles, and there is clear evidence of LV remodeling in endurance athletes, it should not be surprising that the RV also remodels

If there was no proportionate rise in RV volume, then there would be a non-sustainable mismatch in what is essentially a closed-loop model. Scharhag and his colleagues provided evidence of balanced bi-ventricular remodeling in elite endurance athletes using MRI images. Although the RV's resting afterload is considerably less than the LV in absolute terms, the increase in exercise pulmonary artery pressure is comparatively higher than the increase in systemic arterial pressure.(56,57).This increase in RV afterload is associated with both the pulmonary artery's inelastic properties and a relative lack of pulmonary circulation vasodilatation. Accordingly, like the LV, in athletes performing large volumes of endurance training, there is a major incentive for RV enlargement. Actually, in resistance-trained athletes, less is known about RV remodeling and this needs more study.(58)

Exercise in healthy populations may also be an important determinant of RV function. Complex ventricular arrhythmias are commonly associated with RV structural and functional abnormalities in elite endurance athletes, but not with the left ventricle (LV) This syndrome occurs mainly in those who conduct the most strenuous exercise intensity and is not clarified by family predisposition, indicating that exercise may play a direct role in RV remodeling (26). Nonetheless, earlier accounts of athletic cardiac remodeling, called the heart of athletes, focused mainly on LV.(57,59)

Aaron et al.(60) demonstrated in a broad nonathletic population that end-diastolic volumes of RV mass and RV increased with the level of physical activity, independent of LV measurements. This is consistent with some animal studies where intensive exercise contributed to a disproportionate increase in RV mass relative to LV. In endurance athletes, when evaluated immediately after intense prolonged exercise, acute

changes in RV structure and function are more prevalent and deeper than for the LV. By contrast, the few studies that have chronic structural RV remodeling in athletes have shown volume and mass increases proportional to those of the LV (56,61)

Cardiac Mechanics

Recently, new technology has made it possible to determine the dynamics underlying LV function (e.g. deformation of the myocardium in the longitudinal, radial and circumferential planes, and counter directional rotation of the ventricular base and apex).Cardiac mechanics are intimately linked to the underlying myocardial architecture, which in response to exercise training, as outlined above, significantly remodels. Consequently, authors have sought to investigate the effect of exercise training on LV mechanics. This is an emerging field, but early data indicate a lower resting mechanics for highly fit individuals.(62,63)

Compared to the bradycardia caused by endurance training, a lower degree of myocardial deformation in rest is likely to make it easier to draw on a greater reserve during exercise. Recent work has shown that this adaptation is likely to rely on the length of the training experience in ventricular mechanics. LV rotational mechanics appear to increase during the initial phase of athletic training, possibly related to an increased blood volume, which is then accompanied by normalization, or even reduction, of mechanics once the myocardium itself has been remodeled.(64)

6. METHODOLOGY

6.1 Study Design

Following treatment for an acute coronary syndrome (ACS), once medically stable on optimal medical therapy and fit for discharge, patients were recruited for a cardiac rehabilitation program. All adult patients who were 65 years old and below, presenting to our institution with ACS and willing to undergo cardiac rehabilitation were enrolled in the study after obtaining written consent. Participants with contraindications to exercise testing and training were excluded from the study.

6.2 Baseline pre-randomization assessment:

All enrolled participants and their caretakers or immediate family members were educated on their patient's cardiac status, the coronary risk factors that predispose them to acute coronary events and how to modify them positively to prevent a recurrence. All patients underwent baseline echocardiographic and functional assessments between week zero and week one. Based on LV ejection fraction, assessed by transthoracic echocardiogram done pre-discharge, these participants were initially stratified, into two groups – those with LVEF >40% and those with LVEF < 40%. All patients then underwent a symptom-limited pre-discharge Bruce protocol exercise stress test and/ 6minute walk test, to have baseline documentation of their functional capacity.

6.3 Randomization followed by an active phase of the study

They were then randomized into intervention group and controls by block randomization using a concealed envelope method. During the active phase, both the intervention group and the controls were advised to lead a physically active lifestyle

with graded exercises. Intervention group received a 12-week structured exercise program of 2-3 sessions per week of supervised AIT in addition to the standard post-AMI care whereas the controls received the standard post-AMI care as per the current institutional practice. Controls were encouraged to walk daily for at least half an hour with an aim to achieve a consistent walking speed of 3-4kms in half an hour by 12 weeks.

6.4 Exercise protocol for the intervention group:

The exercise protocol followed for the intervention group were supervised, centre-based, thrice-weekly sessions of Aerobic Interval Training (AIT) with a target goal of completing 36 sessions in 3-4 months' time. Each session consists of 10 minutes of warm followed by AIT for 30-45 minutes followed by 10 mins of cool down.

AIT was administered in two modes: -

- Treadmill Based Aerobic Interval Training
- Step Aerobics based Interval Training.

AIT protocol consisted of a warm-up period of 10 minutes followed by 30-45 minutes of Interval training consisting of 1-2 minutes of high-intensity exercise alternating with 1 minute of active recovery culminating with a cool-off period of 3-5 minutes. Resting heart rates and blood pressures were measured at the beginning and end of each exercise session. Heart rates were measured via the treadmill machine and using a heart rate sensor on the chest and its monitor worn as a wristwatch. The targets for warm-up, active exercise, active recovery and cool-off period were 60-70% Maximum Peak Heart Rate (MPR), 90-95%MPR, 50-70%MPR and 50-70% MPR respectively. (MPR was calculated for all the intervention group using the formula, MPR = 220 - age.) These

targets were achieved in a graded fashion within the three-month period, tailored according to the baseline exercise capacity of each patient. After completion of the 12-week AIT, an endurance test was performed on all intervention group.

6.5 Final assessments:

Both the intervention group and the controls were assessed at baseline and at 3 months for the following parameters.

1) *Functional capacity*, as measured by the following variables – Resting heart rate, Exercise duration, Metabolic Equivalents (METs), Heart rate recovery at 1 min (HRR) assessed by Bruce protocol exercise stress test and 6min Walk Distance (6MWD)

2) *Cardiac function*, as measured by ECHO parameters – (a) LV volumes, LV ejection fraction, LV global longitudinal strain (GLS), LV septal E/e' and LV wall motion score index and (b) RV function parameters TAPSE and RVS'. The echocardiogram was performed using GE-VIVID E9 echo machine, by experienced staff echocardiographers, who were blinded to the patient's randomization group.

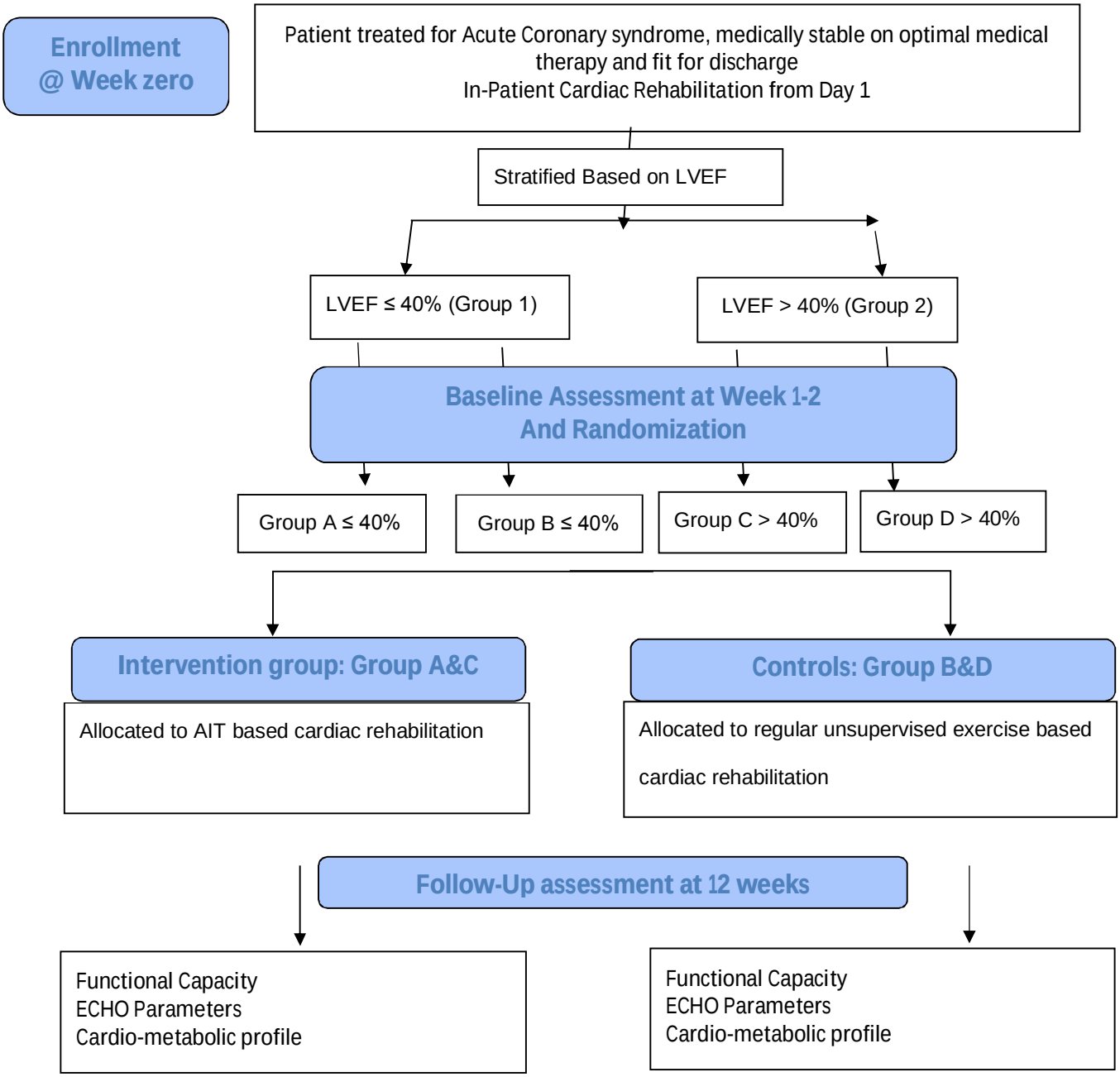
3) *Cardiometabolic profile*, as assessed with the following variables - blood pressure, blood sugar, lipid profile, body mass index (BMI) and waist-hip ratio (WHR).

Hence a randomized controlled trial to assess the differential benefit of AIT on post-AMI patients stable on optimal medical therapy and stratified based on a baseline LV ejection fraction was conducted.

6.6 Setting:

The study was conducted from March 2018 to July 2019, in the Department of Cardiology, Christian Medical College, Vellore.

6.7 Flow Chart Of Study Design



6.8 Participants

6.8.1 Inclusion criteria:

All adult participants who are 65 years of age or below, treated for acute coronary syndrome and medically stable on optimal medical therapy at discharge and willing to consent to participate in an exercise-based cardiac rehabilitation program were eligible for the study.

6.8.2 Exclusion criteria:

Patients with the following criteria were excluded from the study

1. Participants with cardiac contraindications to treadmill testing - Unstable angina, Uncontrolled HTN (SBP >160 &/or DBP >100mmHg), Uncontrolled dysrhythmias, Decompensated heart failure (not evaluated or effectively treated), Severe stenotic or regurgitant valvular disease and Hypertrophic cardiomyopathy
2. Participants who are physically unable to walk - suffering from injuries or arthritis of the lower limb and spine, and myoneuropathies
3. Acute infection or related symptoms
4. Living more than 30kms away from the hospital
5. Not willing to attend follow up clinics.

6.9 Outcome Measures:

Primary Outcome:

1. *Functional capacity* as measured by (a) METS (Metabolic Equivalents) (b) Heart rate recovery at 1 min (HRR) and (c) 6min Walk Distance (6MWD)
2. *Cardiac function*, as measured by echocardiographic parameters (a) LV volumes and LV ejection fraction, (b) LV global longitudinal strain (GLS), (c) LV Septal E/e' and (d) RV function parameters TAPSE and RVS'.

Secondary Outcome/s:

1. Improvement in cardio-metabolic profile (blood sugars, lipid profile)
2. Improvement in Waist to Hip Ratio (WHR) and or Body Mass Index (BMI)
3. Decreased resting heart rate and blood pressure

6.10 Statistical Analysis:

6.10.1 Calculation of Sample size:

From the reference, the study cited, the change from pre to post EF in the exercise group and control group was calculated([post-pre]/pre). The exercise group had a 20% increase from baseline, whereas the control had a 10% increase from baseline. Thus considering a difference of 10% among the two groups with an assumed standard deviation(SD) of 20%, with a power of 80 and 5% alpha error, we need a sample of 64 in each group i.e., a total of 256.

6.10.2 Statistical Methods:

Categorical variables were summarized using counts and percentages. Quantitative variables were summarized using mean and standard deviation or median and IQR. Chi-

square test was used to compare the proportions of the categorical variables among the groups. Two sample t-test/Mann-Whitney U tests were used to compare the continuous variables between the two groups. The pre-post change was calculated for both primary and secondary outcomes. The change was compared using Independent-t-test among the two groups. The difference in change among the two groups was presented with 95% CI to show the effect

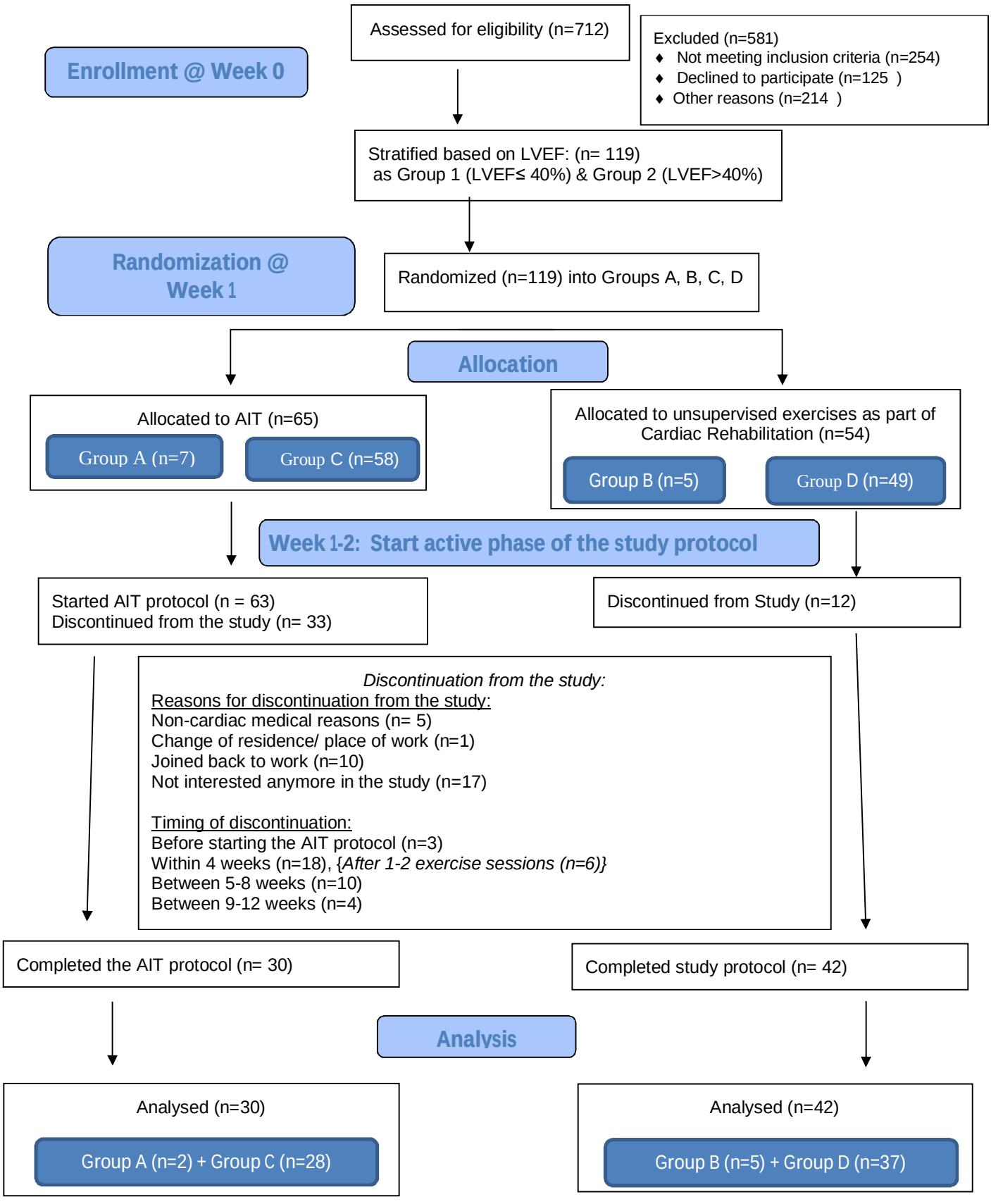
7. RESULTS

712 patients were screened for enrollment into the study and 119 patients who fulfilled the inclusion and exclusion criteria were recruited into the study. 581 screened patients were excluded for reasons of age more than 65, usual residence in a different state, remote location of the home within the state, work commitments, not medically stable, planned for CABG or not willing to participate.

The recruited patients were then stratified based on LVEF and subsequently randomized into 65 intervention group and 54 controls. But 35 patients from the intervention group (intervention group) and 12 patients from the control group (controls*)* dropped out of the study. Of the 35 patients, 3 dropped out even before the start of the active phase. Among the remaining 32, six dropped out within 1 or 2 exercise sessions and 13 within 2 weeks.

Sheer unwillingness to be involved any further in the study was the cited reason for most of them. 18 participants withdrew from the study because of noncardiac medical reasons. Thus 30 intervention group and 42 controls completed the 12-week intervention study and the pre and post-intervention data were analyzed for them.

7.1 Flow Chart of Study Protocol



7.2 Baseline characteristics

The mean age of patients was 50.72 (9.83) among intervention group and 54.15 (9.59) among controls, (P=0.06). The sex ratio was skewed in favour of men in both the groups – 59 men, 6 women among intervention group and 46 men, 8 women among controls. Over 90% of these patients were non-vegetarians. There were more smokers and hypertensives among the intervention group than among the controls, but the distribution of diabetics had a contrary pattern. 59% among intervention group and 76% among controls were diabetics. Regression analysis suggested no significant influence on the outcome data. Among the various traditional coronary risk factors, we found that dyslipidemia and diabetes mellitus was seen in 73% and 66% respectively of the participants whereas hypertension was seen in 37% and chronic smoking among 32%. None of them reported a family history of premature coronary artery disease. The average baseline weight was 71.45kg among intervention group and 67.8kg among controls.

79% of participants had ST elevation myocardial infarction (STEMI), whereas 21%, had Non-ST elevation myocardial infarction (NSTEMI). Coronary artery disease (CAD) among the participants had a distribution as given - single vessel disease (SVD) was seen in 54%, double vessel disease (DVD) in 31%, triple vessel disease (TVD) in 9% and minor coronaries in 6%. Coronary angioplasty was performed in over 90% of participants (90% in controls and 89% in intervention group) whereas 7% had just medical management.

The baseline data on demography, clinical characteristics, functional capacity and echocardiographic parameters are as shown in Table1

7.3 Study Results:

7.3.1 Exercise Targets achieved: Through the patient-tailored graded AIT program, all 30-intervention group consistently achieved 80% MPR whereas 67% achieved 95% MPR or more while 13 of them achieved 100% of MPR. (Table 2)

7.3.2 Compliance: The study protocol suggested completing 36 exercise sessions in 3-4 months. 80% of intervention group (n=24) completed the study with good compliance, in 3 to 5 months' time and the remaining 20% completed 36 sessions in 6-7 months' time. (Table 3). Based on this, the intervention group (n = 30) were further classified as good compliance group (n=24) and a poor compliance group (n=6) (Table 3)

7.3.3 Endurance test: At the end of 36 sessions, an endurance of each patient was measured in terms of ability to run continuously a distance from 3kms up to 10kms at speeds varying from 4.5kmph to 8kmph. All the 30 patients in the intervention group in the AIT (100%) were able to run 3kms, 77% were able to run 5kms and 20% ran up to 10kms. (Table 4)

7.3.4 Functional Capacity:

6min Walk Distance (6-MWD), Resting heart rate, Treadmill Test (TMT) variables – exercise duration, metabolic equivalents (METs) achieved and Heart Rate Recovery (HRR) at 1 minute on a Bruce exercise protocol were measured as indicators of functional capacity both at baseline and at the end of the 12 week program, both among the intervention group and controls. A comparison was then made between the mean

difference in functional capacity among intervention group and controls which are as shown in Table 5.

Both intervention group and controls demonstrated an improvement in functional capacity at the end of 3 months, however, the magnitude of improvement was much more among the intervention group and this was statistically significant. The resting heart rate dropped by 16 beats per minute among the intervention group, whereas it showed a slight rise among the controls. This was a statistically significant difference.

6-minute walk distance among the interventional group rose to a mean of 104 meters whereas it only rose to 50 meters among the controls.

Heart rate recovery at 1 minute improved in both intervention group and controls - a mean improvement of 6.4 beats per minute in intervention group against a mean improvement of 3.4 beats per minute among controls. Although this was numerically higher among intervention group, the difference between intervention group and controls were not statistically significant.

The exercise duration and METs achieved improved by a mean of 3.5 among intervention group whereas it improved only by a mean of 1 among the controls.

Duke Treadmill Score (DTS) also showed a remarkable improvement among intervention group as compared to the controls.

7.3.5 Echo Parameters:

Multiple echo parameters were measured to assess the impact of AIT on reverse LV remodelling. Indices of LV function - LVEF, LVESV and LV-GLS and marker of RV function – Tricuspid annular plane systolic excursion (TAPSE) improved in all patients. This improvement was more among the intervention group than controls but was statistically not significant. However, when the intervention group with good compliance to AIT protocol (n=24) were compared against the controls (n=42), LVEF, LV-GLS and RV-TAPSE were statistically significantly better among the intervention group.

LVEF improved by 6.5% among controls, 10.6% among intervention group and 13.6% among intervention group with good compliance. The more sensitive index of LV function – LVGLS improved by 9.2%, 14% and 18% among controls, intervention group and intervention group with good compliance respectively. TAPSE, a marker of RV function showed a similar finding. It improved by 3.2%, 12.5% and 15.1% among controls, intervention group and intervention group with good compliance respectively.

LV WMI (LV wall motion index) reduced in both the groups. The scoring index showed a reduction of 1.7% among controls, 10% among intervention group and 12.2% among good compliance group. Although not statistically significant, LVWMI showed a trend towards improvement in the AIT group.

LV septal E/e', an indirect measure of LV filling pressures and therefore diastolic function, decreased in both controls and intervention group and the change was not

statistically significant. Other echocardiographic parameters also showed no significant difference between the two groups (Table 6).

7.3.6 Cardio-metabolic profile:

With AIT, all participants achieved a reduction in anthropometric parameters – body weight, BMI and waist circumference. The reduction in weight and BMI were significantly lower among intervention group than controls. The reduction was far more pronounced in patients who underwent AIT with good compliance. While the intervention group lost a mean of 1.52kgs through the AIT, the controls gained a mean of 0.7kgs. This corresponded to a reduction in BMI among intervention group by 0.55 and increase by 0.27 among controls.

Waist circumference decreased by 1.20cms among intervention group while it increased by 0.56cms among controls. In both groups, there is a improvement in glycemic control among diabetes as measured by HbA1c and Lipid profile. However, there was no statistical significance between intervention group and controls.

Tables and Graphs

7.3.7 Table 1: Demography and Clinical Characters

Baseline Variable	*intervention group n (%)*	*Controls n (%)*	*P Value*
GENDER			
Male	59 (91)	46 (85)	P=0.347
Female	6 (9)	8 (15)	
RISK FACTORS			
Non vegetarian	58(91)	52(96)	P=0.222
vegetarian	6(9)	2(4)	
Smokers	24(38)	14(26)	P=0.350
Nonsmokers	33(52)	35(65)	
Ex-smokers	6(10)	5(9)	
Alcoholics	15(24)	13(24)	P=0.994
Non-Alcoholics	43(68)	37(69)	
Ex-alcoholics	5(8)	4(7)	
Diabetes	38(59)	41(76)	P=0.057
Non-Diabetes	26(41)	13(24)	
Hypertension	26(40)	18(33)	P=0.453
Non-Hypertension	39(60)	36(67)	
Dyslipidemia	47(72)	40(74)	P=0.829
Non-Dyslipidemia	18(28)	14(26)	
DIAGNOSIS			
NSTEMI	16(25)	9(17)	P=0.270
STEMI	48(75)	45(83)	
NO OF VESSELS			
SVD	34(53)	29(55)	P=0.367
DVD	19(30)	17(32)	
TVD	5(8)	6(11)	
Minor Coronary	6(9)	1(2)	
TREATMENT			
Angioplasty	58(89)	50(92)	P=0.032
Thrombolysis	1(2)	2(4)	
Medical Rx	6(9)	2(4)	

Baseline Variable	*intervention group Mean (SD)*	*Controls Mean (SD)*	*P Value*
Age	50.72(9.83)	54.15(9.59)	0.06
Working days	5.75(1.26)	5.27(2.24)	0.15
No of Tea/coffee per day	3.42(2.04)	3.23(2.51)	0.64
No of days Eating Non-Veg per week	1.67(1.63)	1.20(0.79)	0.02
ANTHROPOMETRY			
Weight	71.45(11.35)	67.8(12.40)	0.10
Body mass Index (BMI)	25.59(3.80)	24.85(3.71)	0.30
Waist Hip Ratio (WHR)	0.98(0.07)	0.99(0.06)	0.40
ECHO PARAMETERS			
LV EF	54.12(10.01)	52.46(8.33)	0.33
LV ESV	29.30(10.5)	30.00(11.43)	0.72
LV EDV	63.87(18.17)	62.61(17.56)	0.70
LV e/e'	11.43(3.12)	12.77(4.71)	0.07
LV WMSI	1.18(0.29)	1.20(0.23)	0.65
LV GLS	15.59(3.54)	14.89(3.59)	0.29
RV S'	11.23(2.02)	11.39(2.07)	0.66
RV TAPSE	19.72(2.98)	19.46(3.70)	0.67
TR grdt Peak	12.13(6.2)	12.36(5.25)	0.83
TREADMILL PARAMETERS			
Exercise duration	6.25(2.36)	5.36(2.16)	0.04
METs achieved	8.38(2.34)	7.53(2.06)	0.04
TMT Duke score	7.09(2.54)	6.38(2.18)	0.11
Heart Rate recovery at 1 min	26.56(16.13)	2.92(8.28)	0.14
6-Min walk test distance	400.14(86.34)	403.61(79.05)	0.82
Resting Heart rate	84.30(11.84)	86.98(12.68)	0.24

7.3.8 Table 2: Exercise targets achieved

Percentage MHR	intervention group (A and C) n (%)
80%	30(100)
90%	26(87)
95%	20(67)
100%	13(43)

7.3.9 Table 3: Compliance to 36 exercise sessions:

No of Months to complete AIT	Intervention group n (%)	
3	14(47)	Good Compliance (80%) (n=24)
4	6(20)	
5	4(13)	
6	2(7)	Poor Compliance (20%) (n=6)
7	4(13)	

7.3.10 Table 4: Results of endurance test:

Distance in kms	Intervention group n (%)
3	30 (100)
4	28 (93)
5	23 (77)
8	8 (27)
10	6 (20)

7.3.11 Table 5: Change in functional capacity among intervention group and controls

Variables	*All Intervention group (n=30) Mean Difference (SD)*	*Controls (n=42) Mean Difference (SD)*	*P-Value*
Resting Heart rate	-16.23(8.26)	+0.51(11.49)	<**0.01**
Exercise duration (TMT)	+3.46(1.85)	+1.14(1.64)	**0.04**
METS achieved (TMT)	+3.57(2.16)	+1.24(1.62)	<**0.01**
Duke score (TMT)	+3.53(2.29)	+0.49(1.64)	<**0.01**
Heart Rate Recovery at 1 min (HRR)	+6.43(10.94)	+3.36(9.68)	0.22
6-Min walk distance(m)	+104.70(85.29)	+50.40(62.96)	**0.0031**

Post-intervention Variables	*Intervention group with good compliance (n=24) Mean Difference (SD)*	*Controls (n=42) Mean Difference (SD)*	*P-Value*
Resting Heart rate	-17.21(8.31)	+0.51(11.49)	<**0.01**
Exercise duration	+3.65(1.91)	+1.14(1.64)	<**0.01**
METs achieved (TMT)	+3.78(2.26)	+1.24(1.62)	<**0.01**
Duke score (TMT)	+3.79(2.34)	+0.49(1.64)	<**0.01**
Heart Rate Recovery at 1 min (HRR)	+7.25(11.49)	+3.36(9.68)	0.15
6-Min walk test distance	+109.38(92.37)	+50.40(62.96)	**0.0034**

7.3.11 Table 6: Change in echo parameters among intervention group and controls

Baseline Variable	Controls (n=42) B&D Mean Difference (SD)	Intervention group (n=30) A&C Mean Difference (SD)	P Value	Intervention group (n=24) A&C Mean Difference (SD)	P Value
LV EF	+3.41(6.27)	+5.79(6.34)	0.33	+7.19(6.11)	**0.0231**
LV GLS	+1.38(2.38)	+2.17(2.51)	0.29	+2.70(2.27)	**0.0328**
RV TAPSE	+0.62(3.42)	+2.47(3.89)	0.67	+2.93(3.94)	**0.0157**
LV ESV	-2.97(8.30)	-3.62(8.61)	0.72	-4.09(9.24)	0.6166
LV EDV	-3.00(12.33)	+0.32(18.99)	0.70	+1.25(20.38)	0.2979
LV WMSI	-0.02(0.26)	-0.12(0.21)	0.65	-0.15(0.23)	0.0608
LV e/e'	-0.22(3.05)	-0.07(2.55)	0.07	+0.02(2.75)	0.7559
RV S’	-0.21(2.25)	+0.29(2.08)	0.66	+0.68(1.79)	0.1056
TR grdt Peak	-0.22(6.75)	+1.14(6.41)	0.83	+1.94(6.69)	0.2242

7.3.12 Table 7: Changes in cardiometabolic parameters among intervention group and controls

Post intervention Variables	*Intervention group (n=30) Mean Difference (SD)*	*Controls (n=42) Mean Difference (SD)*	*P Value*
Weight	-1.52(2.48)	+0.69(3.45)	**0.0038**
Body mass Index (BMI)	-0.55(0.92)	+0.27(1.32)	**0.0046**
Waist Circumference	-1.20(4.82)	+0.56(3.18)	0.0678

Post-intervention Variables	*Intervention group with Good compliance (n=24) Mean Difference (SD)*	*Controls (n=42) Mean Difference (SD)*	*P Value*
Weight	-1.74(2.69)	+0.69(3.45)	**0.0043**
Body mass Index (BMI)	-0.63(1.00)	+0.27(1.32)	**0.0053**
Waist Circumference	-1.71(5.13)	+0.56(3.18)	**0.0310**

7.3.13 Table 8: Changes in cardiometabolic parameters among intervention group and controls

Post intervention Variables	*Intervention group A&C (n=30) Mean Difference (SD)*	*Controls B&D (n=42) Mean Difference (SD)*	*P Value*
Total Cholesterol	-59.17 (37.54)	-63.95(42.19)	0.62
Triglycerides	-45.13 (82.84)	-54.39(109.79)	0.69
High density lipoprotein (HDL)	-2.10(6.00)	-2.05(6.58)	0.97
Low density lipoprotein (LDL)	-54.53(27.61)	-59.90(38.71)	0.51
HbA1c	-0.65(1.30)	-0.98(2.10)	0.46

Post intervention Variables	*Intervention group with Good compliance A&C (n=24) Mean Difference (SD)*	*Controls B&D (n=42) Mean Difference (SD)*	*P Value*
Total Cholesterol	-66.29(35.62)	-63.95(42.19)	0.82
Triglycerides	-48.33(80.57)	-54.39(109.79)	0.81
High density lipoprotein (HDL)	-3.00(4.99)	-2.05(6.58)	0.54
Low density lipoprotein (LDL)	-56.96(27.69)	-59.90(38.71)	0.74
HbA1c	-0.86	-0.98(2.10)	0.80

7.3.14 Figure 1: Change in Functional capacity with AIT on 6MWT

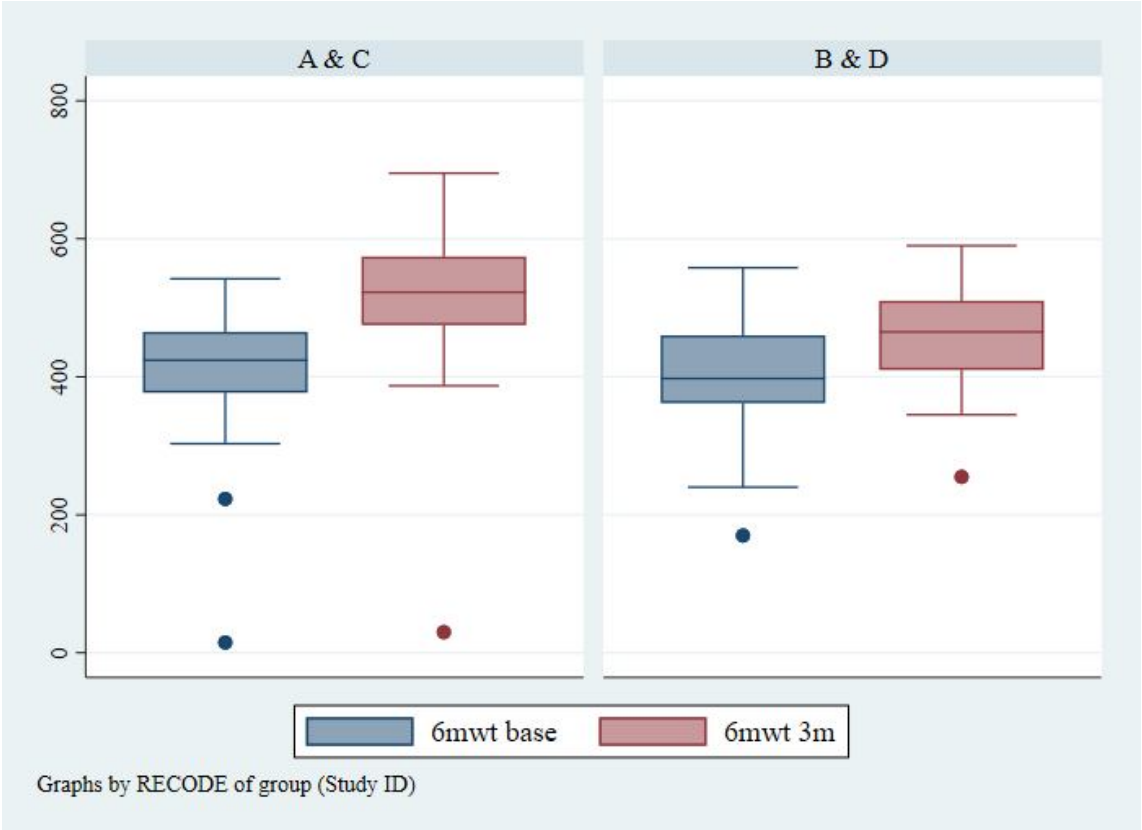


Figure 1 Showing

- In Intervention groups (A&C) mean 6MWT before and after is 408 meters and 512 meters respectively. Improvement of 104 meters was observed.
- Among Control Groups (B&D) mean 6MWT before and after is 400 meters and 450 meters. Improvement of 50 meters was observed

7.3.15 Figure 2: Change in Functional capacity with AIT on 6MWT

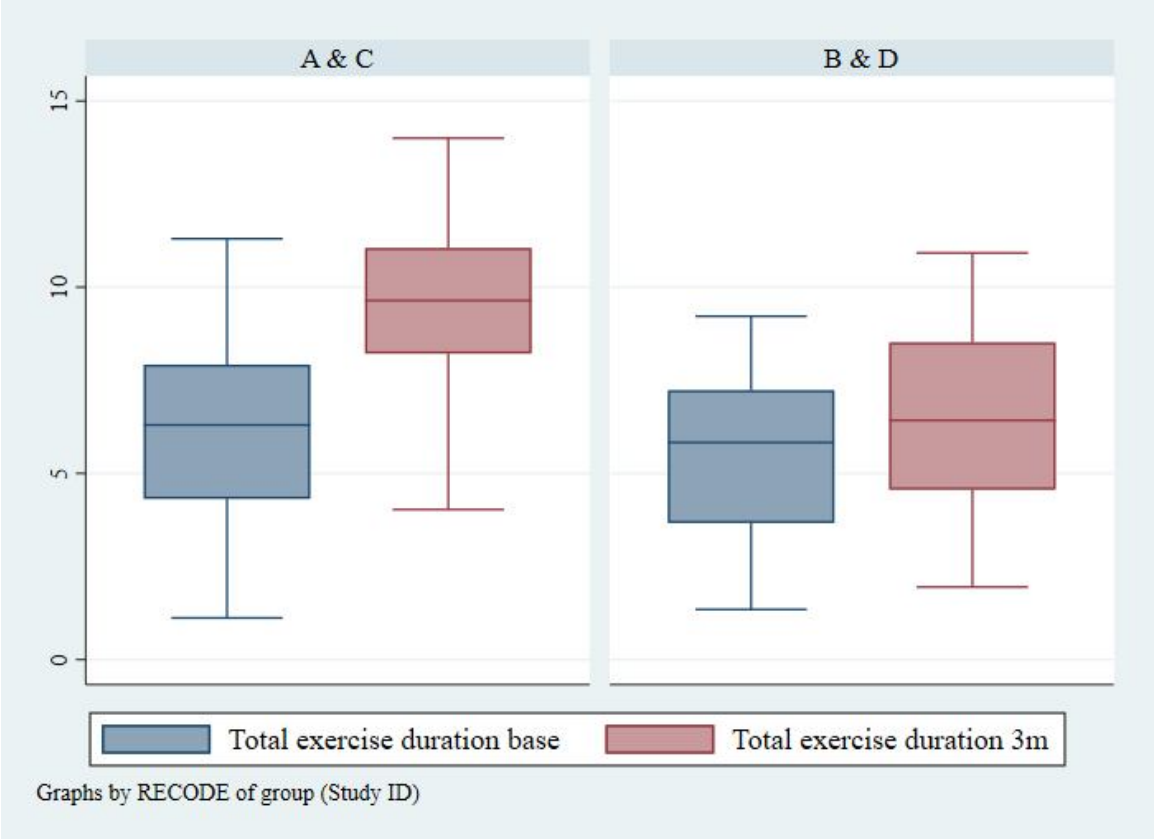


Figure 2 Showing

- In Intervention groups (A&C) the mean TMT duration before and after is 6.22 minutes and 9.68 minutes respectively. Improvement of 3.46 minutes was observed.
- Among Control Groups (B&D) mean TMT duration before and after is 5.42 minutes and 450 meters. Improvement of 6.61 minutes was observed

7.3.16 Figure 3: Change in Duke prognostic score with AIT

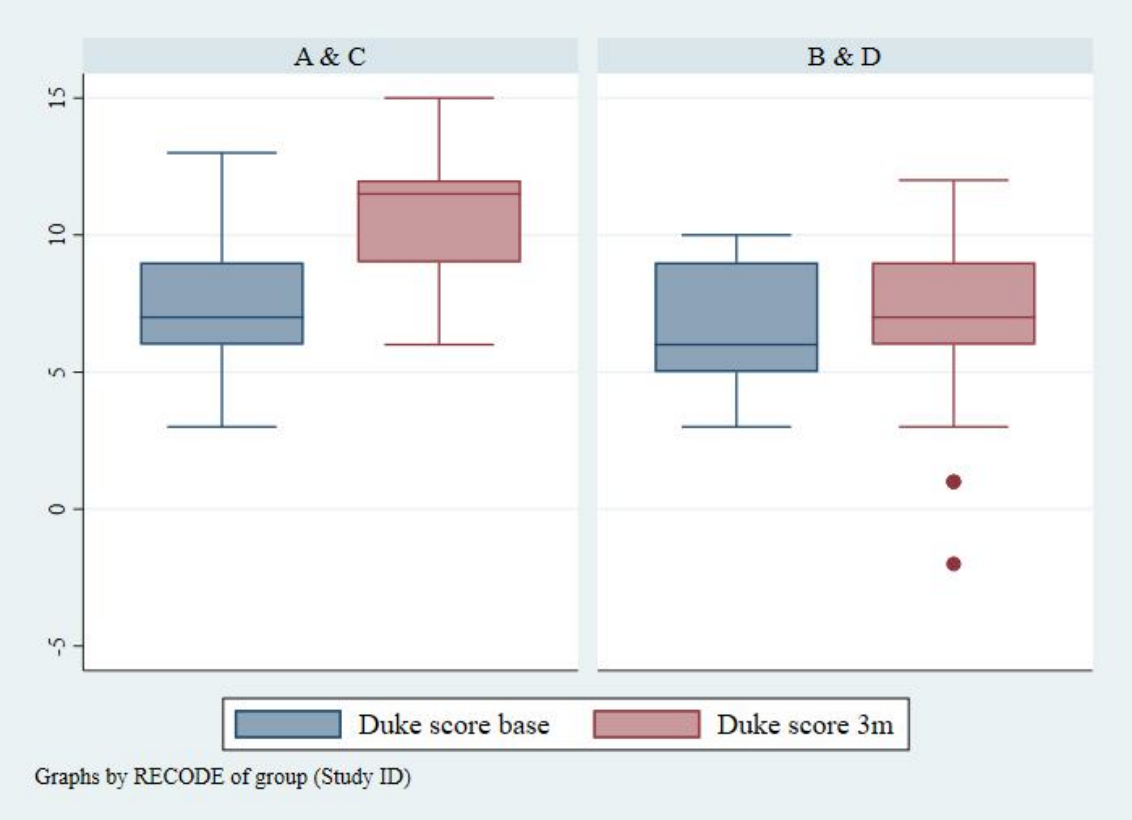


Figure 3 Showing

- In Intervention groups (A&C) the mean Duke prognostic score before and after is 7.37 and 10.90 respectively. Improvement of 3.53 score was observed.
- Among Control Groups (B&D) mean Duke prognostic score before and after is 6.53 and 7.0 respectively. Improvement of 0.49 score was observed

7.3.17 Figure 4: Change in LV EF with AIT

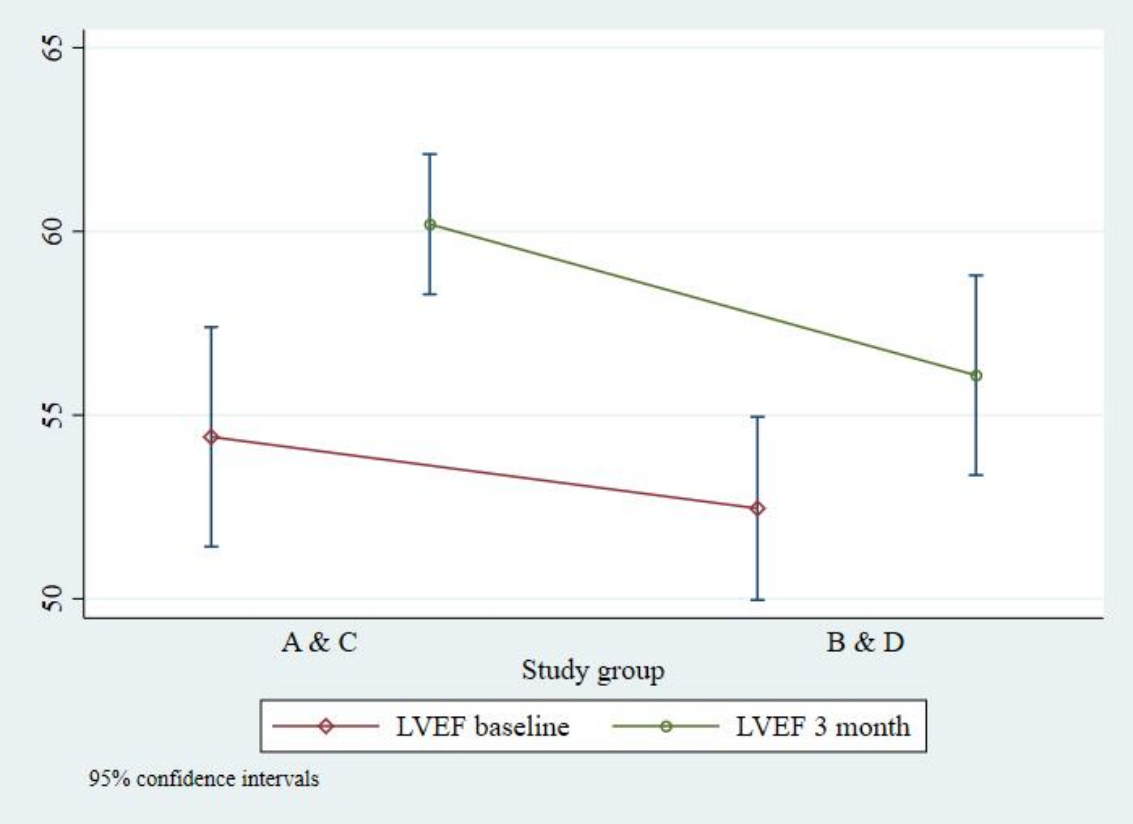


Figure 4 Showing

- LV Ejection fraction improvement by 13.6 % In the Intervention groups with good compliance (A&C). The mean EF before and after were 52.84% and 60.02% respectively
- Among Control Groups (B&D) mean EF improved by 6.5%. The mean EF before and after were 52.48% and 55.95% respectively.

7.3.18 Figure 5: Change in LV Global Longitudinal Strain with AIT

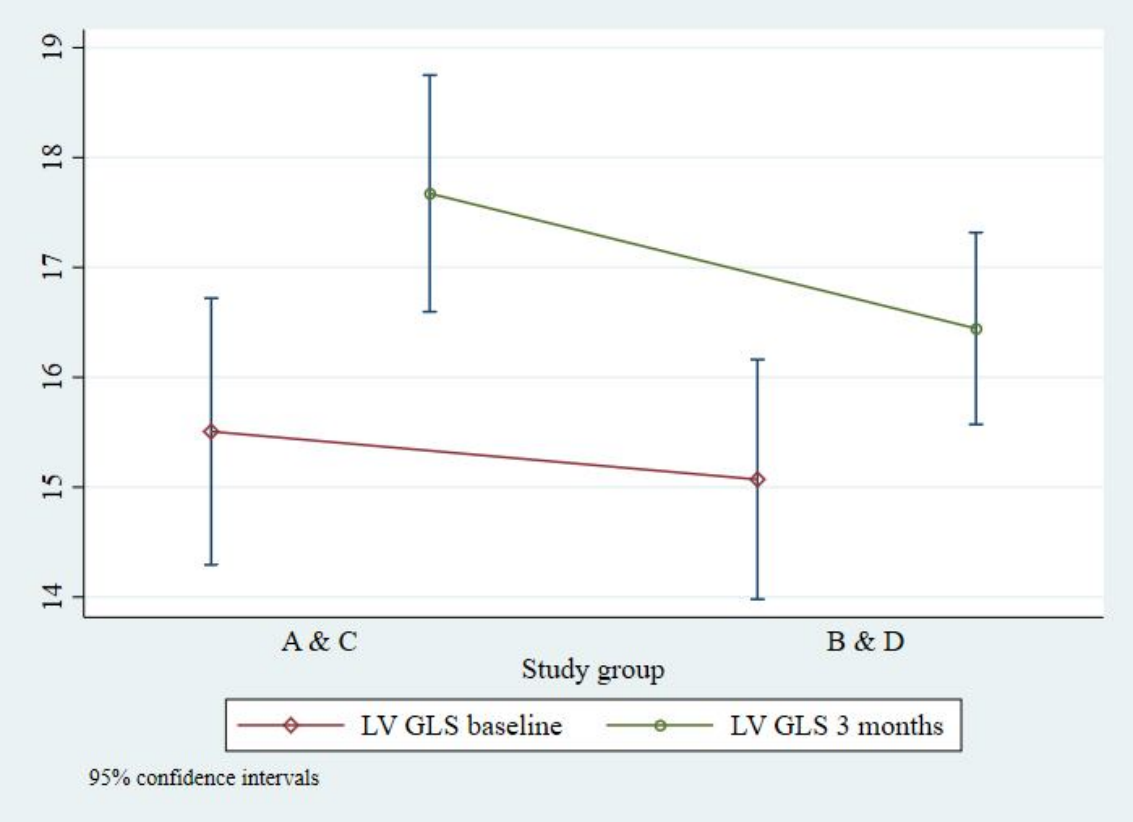


Figure 5 Showing

- LV Global longitudinal strain has increased by 18 % In the Intervention groups with good compliance (A&C). The mean LV GLS before and after were 14.98 and 17.68 respectively
- LV GLS among controls improved by 9.2%. The mean LV GLS before and after were 15.03 and 16.44 respectively

7.3.19 Figure 6: Change in End Systolic with AIT

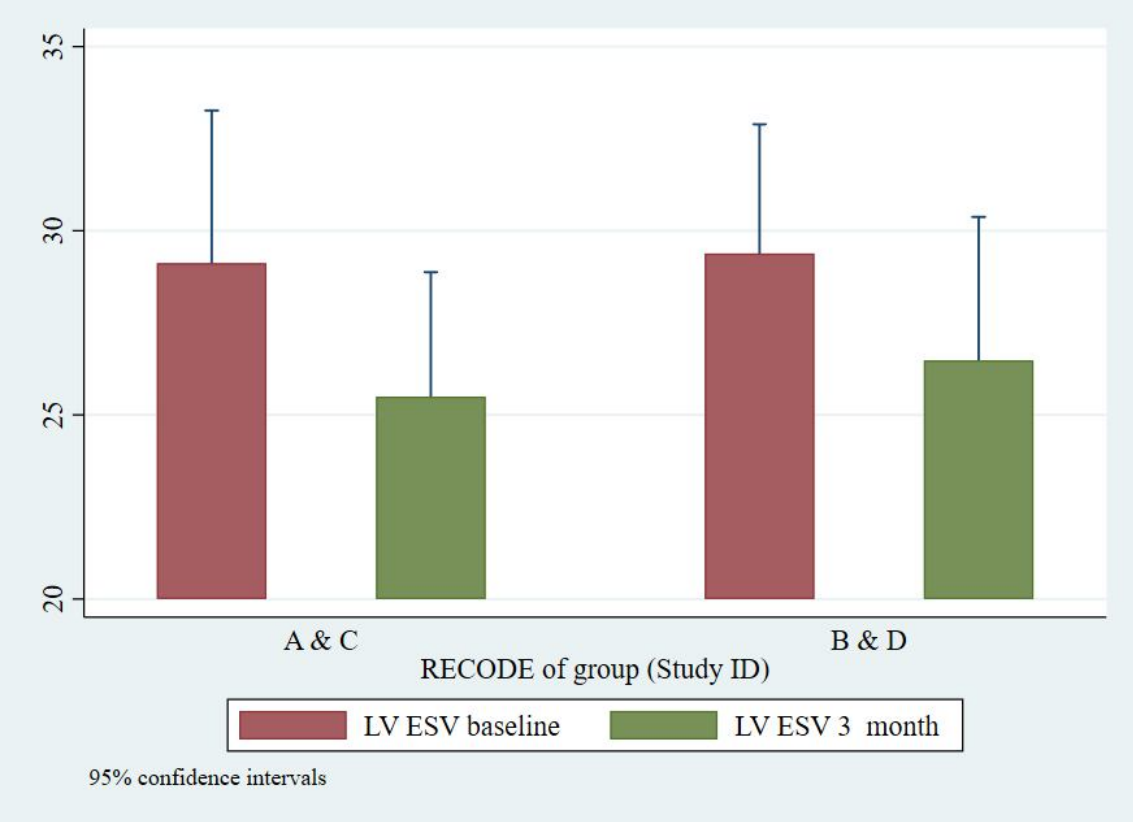


Figure 6 Showing

- There is a Reduction in End Systolic volume in both Intervention groups with good compliance (A&C) and Control Groups (B&D). 13.28% reduction is seen in Intervention Groups, while controls had a reduction by 10%

7.3.20 Figure 7: Change in End Diastolic Volumes with AIT

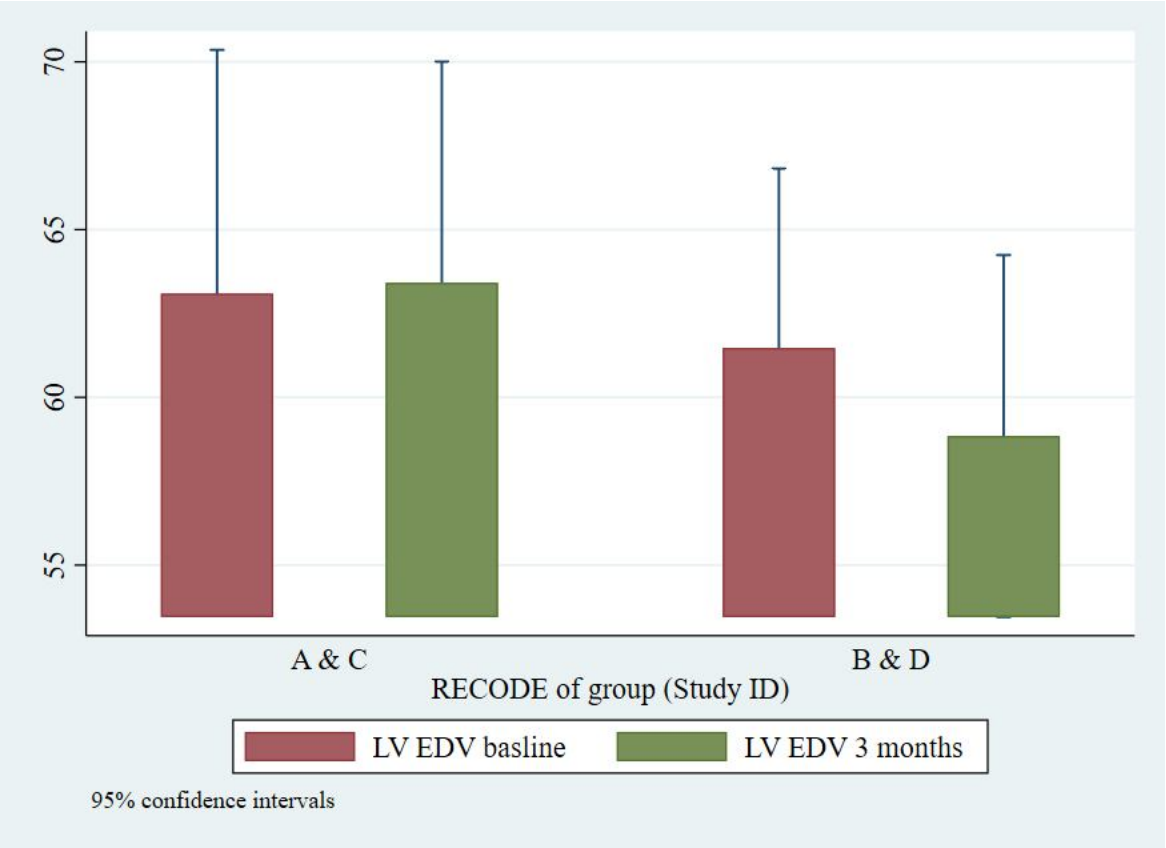


Figure 7 Showing

- In Intervention groups with good compliance (A&C) there is increase in End diastolic volume after the intervention by 1.93%. In controls there is a reduction by 4.8%

8. DISCUSSION

Exercise-based cardiac rehabilitation has shown to improve mortality and long-term cardiac prognosis in server earlier studies. Cochrane systematic review and meta-analysis in 2016 demonstrated that an exercise-based cardiac rehabilitation for patients with coronary artery disease resulted in a 26% reduction in cardiovascular mortality and a 18% reduction in hospitalization. Among patients with coronary artery disease, high-intensity interval training (AIT) in comparison to moderate-intensity continuous training, has shown to result in higher cardio-respiratory fitness among patients from the developed world.

However, data on its effects on LV reverse remodelling following an MI is limited. Hence this study was conducted to observe if AIT can produce a higher cardiorespiratory fitness among patients post-MI and if this would translate into a better reverse remodelling of LV after a myocardial insult.

119 patients who fulfilled the criteria were randomized into the two main arms of the trial – the one which received a supervised, aerobic interval training (65 participants) and another which received an unsupervised exercise training (54 participants). The distribution of baseline parameters was similar in both these groups. Mean age was 50.72 (9.83) among intervention group and 54.15 (9.59) among controls. Women in both groups were equally distributed (6 in intervention group, 8 in controls).

Culturally, middle-aged and older women in India tend to present less often than men to the hospital with any illness, and this is more pronounced among the rural population. Moreover, they generally tend to be unwilling to participate in any interventional trial

which requires them to do regular physical exercises while being supervised by others. A commitment to attend the hospital 2-3 times a week for consecutive 12 -14weeks, during work hours was probably the greatest impediment for our patients to consistently participate in this trial as this would mean loss of that day's wages/ income.

About 71% of participants have not completed higher secondary education. 3% had no formal education, 15% higher secondary education, 22% were graduates, only 5% were postgraduates and 1% studied up to PhD

93% were non-vegetarians while 7% were vegetarians. This could raise the possibility that acute coronary syndrome is much less common among pure vegetarians. This could also be reflective of the changes seen in modern India, as a lesser number of people remain pure vegetarians.

Dyslipidemia and diabetes mellitus were the most common traditional coronary risk factors of coronary artery disease (CAD) identified among the participants – in over two thirds, whereas hypertension and chronic smoking were seen among only one-third of participants. Thus, this identifies the two main targets for population-based strategies to prevent coronary artery disease among even the rural Indians. It was also reassuring to see that smoking was seen only among one-third of the study population. This could be reflective of the benefits of various health education measures that are being carried out for several years, to reduce/ avoid smoking.

Functional Capacity:

Functional capacity is a measure of cardio-respiratory fitness. Randomised trials of exercise training after an MI have suggested that increasing exercise lowers cardiovascular risk. It has been shown that every MET increase in cardio-respiratory fitness translates into improved cardiovascular outcome. Improvement in fitness after 12 weeks of cardiac rehabilitation is shown to be associated with decreased overall mortality - a 13%-point reduction with each MET increase and a 30%-point reduction in those who started with low baseline fitness levels have been demonstrated.

In this study, both intervention group and controls improved in their functional capacity as compared to the baseline, but the improvements in intervention group were significantly more profound than controls. A net gain of 3.57 METs was seen among intervention group while controls had a gain of only 1.24 Mets. This would, therefore, translate into a significant long-term mortality benefit among those who underwent a consistent exercise training. 6-minute walk tests brought out a similar improvement in the functional capacity of patients. There was a 26% improvement in 6-minute walk distance among intervention group whereas the improvement among controls was only 13%.

Duke treadmill score (DTS) is a point system to predict 5-year mortality among patients, using a standard Bruce protocol treadmill testing. It is calculated using the formulae:

DTS = Exercise duration (in minutes) – (5x ST deviation in mm) – (4x angina index).
ST deviation refers to maximum ST change – either elevation or depression, in millimetres measured in any lead except aVR. Angina index gives 0 points for no angina during the test, 1 point for non-limiting angina and 2 points for limiting angina. A score

> 5 indicates a 5-year survival of 97%, a score between 4 and -11 indicate 5-year survival of 90% and a score < -11 indicate a 5-year survival of 65%. In our study, the Duke treadmill score improved by 48% in intervention group, 7% in controls. This indicates a better 5-year survival rate among patients who underwent AIT compared to those who did not.

Cardio-metabolic profile:

With AIT, all participants achieved a reduction in anthropometric parameters of body weight, BMI and waist circumference. The reduction in weight and BMI were significantly lower among intervention group than controls. This confirms the well-known benefit of consistent exercise on weight reduction and therefore improve cardiovascular health.

Lipid profile of both patients and controls improved at the end of 3 months of the study and there was no statistically significant difference seen between the two groups. All patients received statin therapy and most of them at high doses, which probably explains the lack of significant difference between the groups. In this study the extended lipid profile of these patients who has dyslipidemia (20 intervention group vs 33 controls), however, both groups did not show any statistical significance. This can be explained by the impact on statin therapy

Among the diabetes patients, HbA1c of 14 intervention group and 34 controls were analyzed, however, both groups had a marginal reduction of 10% in intervention group

and 13% in controls. As both groups are under the influence of diabetes drugs, there is no statistically significance at the end of the study.

Reverse LV Remodeling:

Reverse LV Remodelling is a term used more often in heart failure or cardiomyopathy, to indicate improvement in cardiac geometry and function. It is classically measured as a reduction in End Systolic Volume (ESV) and an increase in LV Ejection Fraction (LVEF). LV GLS (Global Longitudinal Strain) is one of the recently identified more sensitive indexes of LV function. Hence improvement in LV-GLS would also reflect reverse remodelling of the LV.

In this study, a significant increase in LV-GLS, LVEF, and TAPSE were shown in patients who were compliant to an AIT protocol. However, when all patients who underwent AIT were taken together and compared against the controls, the change was not significant and only a trend towards benefit could be seen. Thus, improvement in the above parameters of biventricular function among intervention group with good compliance may be indicative of the potential of regular AIT to achieve a reversal of LV remodelling following an MI.

9. LIMITATIONS OF THE STUDY

1. The sample size predetermined for the study (n=256) could not be achieved within a limited time period. This may affect the strength of the study. Hence the study should be continued for a longer period to ensure we achieve the sample size and therefore be a better representation of the general population.
2. Although in this study stratification in the intervention group was based on LVEF, only 12 patients with an LVEF < 40% could be recruited into the study. Hence it was not feasible to assess the differential effects of AIT among patients with an LVEF < 40%.
3. Forty-seven participants (39.4%) dropped out of the study – contributing to 53.8% among intervention group and 22.2% among controls. Unfortunately, this may influence the final outcomes of the study.
4. Compliance to AIT was varied among patients, some took 6-7 months to complete the 12-week programme, influencing the results of the group.

10. CONCLUSION:

1. Aerobic Interval Training (AIT) improves the functional capacity and aids to improve the cardiac function in patients post-myocardial Infarction.
2. Good compliance to a 12-week AIT based cardiac rehabilitation, in addition to optimal medical therapy, can result in reverse LV remodelling following myocardial infarction.

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12. APPENDIX

12.1 Supervised Exercise Session Report (IP/OP)

Study ID _____Hospital ID_____ Patient Name _____

Previous Record (Walk/Run): Work speed: _____Rest Speed: _____

Avg Peak HR: _____ Avg Resting HR_____

Session #: ____ Age____ MHR_____THR/RPE: _____Session Date: _____

Phase 1. Reducing Exercise Related Anxiety 2. Optimizing Exercising Capacity
3. Physically Active lifestyle 4. Work resumption

Resting HR_____, Resting BP _____ Warm Up (5 to 10 min)													
	Work Interval Speed	RPE	Work interval Duration	Blood pressure		Average Peak HR		Rest Interval Speed	Rest Interval Duration	Blood pressure		Average Resting HR	
Rep 1													
Rep 2													
Rep 3													
Resting minutes _____Resting HR_____													
Rep4													
Rep5													
Rep6													
Resting minutes _____Resting HR_____													
Rep 7													
Rep 8													
Rep 9													
Resting minutes _____Resting HR_____													
Rep 10													
Rep 11													
Rep 12													
Resting minutes _____Resting HR_____													
Rep 13													
Rep 14													
Rep 15													
Resting minutes _____Resting HR_____													
Rep 16													
Rep 17													
Rep 18													
Cooldown (10 mins)													

12.2 Endurance Test

Study ID _____Hospital ID_____ Patient Name _____

Session #:_____ Age_____ MHR_____ THR: _____ Session Date: _____

Resting HR_____ Resting BP_____

Warm up

	1	2	3	4	5	6	7	8	9	10
SPEED (mph)	Mins	Mins	Mins	Mins	Mins	Mins	Mins	Mins	Mins	Mins
Speed 1										
Speed 2										
Speed 3										
Speed 4										
HR										

Cool Down
HRR@1 min: _____
Resting Bp _____

Total Distance Covered:
Speed 1 _____*1.6*_____(repetitions)=
Speed 2 _____*1.6*_____(repetitions)=
Speed 3 _____*1.6*_____(repetitions)=
Speed 4 _____*1.6*_____(repetitions)=
Total distance=_____

12.3 Target Progress Record

Study ID _____Hospital ID_____ Patient Name _____

80% Target reached on week No_____ Session No_____

90% Target reached on week No_____ Session No_____

95% Target reached on week No_____ Session No_____

100% Target reached on week No _____Session No_____

Above 100% Target reached on week No_____ Session No_____

Endurance Progress Record

Endurance Test 1: Distance covered in Kms _____in _____ (mins) Speeds____

Endurance Test 2: Distance covered in Kms _____in _____ (mins) Speeds ____

Endurance Test 3: Distance covered in Kms _____in _____ (mins) Speeds ____

Endurance Test 4: Distance covered in Kms _____in _____ (mins) Speeds____

Endurance Test 5: Distance covered in Kms _____in _____ (mins) Speeds____

Endurance Test 6: Distance covered in Kms _____in _____ (mins) Speeds ____

Endurance Test 7: Distance covered in Kms _____in _____ (mins) Speeds ____

Endurance Test 8: Distance covered in Kms _____in _____ (mins) Speeds____

Endurance Test 9: Distance covered in Kms _____in _____ (mins) Speeds____

Endurance Test 10: Distance covered in Kms _____in _____ (mins) Speeds ____

12.4 Compliance Record

Sl No	Name	Study ID	Hospital Number	Date of 1st session

No of weeks	Session No	Session No	Session No	Total
Week 1	/01	/02	/03	/3
Week 2	/04	/05	/06	/3
Week 3	/07	/08	/09	/3
Week 4	/10	/11	/12	/3
				Total= /12
Week 5	/13	/14	/15	/3
Week 6	/16	/17	/18	/3
Week 7	/19	/20	/21	/3
Week 8	/22	/23	/24	/3
				Total= /24
Week 9	/25	/26	/27	/3
Week 10	/28	/29	/30	/3
Week 11	/31	/32	/33	/3
Week 12	/34	/35	/36	/3
				Total= /36
Week 13	/37	/38	/39	/3
Week 14	/40	/41	/42	/3
Week 15	/43	/44	/45	/3
Week 16	/46	/47	/48	/3
				Total= /

12.5 Exercise Modes: AIT in Step Aerobics mode and Treadmill mode

13. ANNEXURES

13.1 Patient Information sheet

Title of the Study: Reversal of LV remodelling with Aerobic Interval Training (AIT) in post-MI patients-RCT

Aim: The aim of the study is to increase the Maximum amount of oxygen consumption (VO2 max) and left ventricular (LV) ejection fraction with Aerobic interval training. (AIT)

Methods: Individuals who are treated for acute coronary syndrome in cardiology and who are stable at discharge will be given the option to join the study. History, clinical examination, baseline assessment of functional capacity and Heart reserve will be done by the chief investigator. Each patient undergoes 3 months of exercise-based cardiac rehabilitation programme. At the end of the study the data collected will be analyzed.

Purpose and Explanation of Cardiac Rehabilitation

The cardiac rehabilitation program includes cardiovascular monitoring, physical exercise, dietary counselling, smoking cessation, stress reduction, and health education activities. The levels of exercise that you will perform will be based on the condition of your heart and circulation as determined by the Chief investigator. You will be given exact instructions regarding the amount and kind of exercise you should do. You are advised to participate three times per week in the rehabilitation program. Professionally trained clinical personnel will provide leadership to direct your activities and monitor your electrocardiogram and blood pressure to be certain that you are exercising at the prescribed level. You are expected to attend every session and to follow Chief investigator and staff instructions with regard to any medications that may have been prescribed.

You will be asked to complete the activities unless such symptoms as fatigue, shortness of breath, chest discomfort, or similar occurrences appear. At that point, you will be advised to stop the exercise and inform the program personnel of your symptoms. During the programme, a trained observer will periodically monitor your performance and perhaps take electrocardiogram, pulse, blood pressure, or make other observations for the purpose of monitoring your progress and/or condition. The observer may reduce or stop your exercise program when findings indicate that this should be done for my safety and benefit

Risks

During the Cardiac rehabilitation programme there is the possibility of adverse changes including abnormal blood pressure; fainting; disorders of heart rhythm and very rare instances of heart attack and stroke. Death during cardiac rehab program is even rarer. Every effort will be made to minimize these occurrences by proper staff assessment of your condition before each exercise session, staff supervision during

exercise, and you own careful control of exercise effort. Emergency equipment and personnel are readily available to deal with unusual situations should these occur.

Benefits

Only medical treatment may or may not benefit my health status or physical fitness. Generally, participation in Cardiac Rehabilitation will help determine what recreational and occupational activities you can safely and comfortably perform. Many individuals in such programs also show improvements in their capacity for physical work. For those who are overweight and able to follow the physician's and dietitian's recommended dietary plan, this program may also aid in achieving appropriate weight control.

Compensation for participation:

Since there is no direct or indirect chance of risk causing an increase in disability or death, there is no such provision for compensation.

What happens if you choose to withdraw from study participation?

Participation in the study will be voluntary. There will be no change in treatment or future management even if the person involved withdraws from the study. The information gained will not be used for any publication or study purpose.

Confidentiality:

All the data collected will be stored in the computer in a separate folder which will be password protected. This computer will only be accessed by the primary investigator. Each participant will be assigned a unique ID while filling the proforma and data entry and further reference will be in relation to this number. Proforma containing the patients' identification details will be kept safe in a locker accessed only by the principal investigator.

Privacy:

Your identity will not be revealed to anyone else as study Id will be the one which will be shared with coinvestigators. Personal identifiers will be removed before the data is sent for publication. However, data of the study may be shared with the Institutional Review Board of Christian Medical College.

Contact information:

If you have any questions about this research study or possibly, please contact:
Dr.Muralidhar B, PG Registrar, Department of PMR, CMC, Vellore- 632004
Phone no: +91- 9390123451, Email: doctor.murali@yahoo.com

13.2 Informed Consent form to participate in a research study

1. **Study Title: :** Effect of Aerobic Interval Training (AIT) in improving functional capacity and LV remodelling in post-MI patients-RCT

Study Number: _____

Subject's Initials: _____ **Subject's Name:** _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree with this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such use is only for the scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

(vi) I am aware of the Audio-visual recording of Informed Consent. [ ]

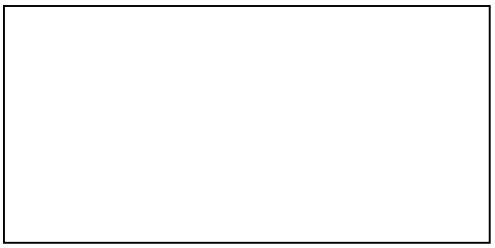
(Click here for Audio Visual guidelines)

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: ____/____/_____

Signatory's Name: _____ Signature:

Or



Representative: _____

Date: ____/____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: ____/____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: ____/____/_____

Name & Address of the Witness: _____

13.3 Proforma

Study ID ☐☐☐☐☐☐☐
Date:

Hospital Number ☐☐☐☐☐☐☐

Name
_____

Sex (Male =1, Female=2) ☐

Date of Birth _____ (dd) _____(mm)_____(yyyy)_____, Age (Completed Years) ☐☐ Years

Address:

_____

Phone (Mobile or Landline)
_____

Demographic Questionnaire

Religion (Hindu=1, Muslim=2, Christian=3, Others=4) ☐

Education in Completed years (No Education=1, Up to 4th Class=2, Up to 10th Class=3, Intermediate=4, Degree=5, PG=6, PhD=7) ☐

Occupation _____

Working days in a Week ☐

Food Habits

Number of Meals (Including Breakfast) per day ☐

Number of Snacks Per day ☐

Number of Tea/Coffee Per day ☐

Food Habits (Non Vegetarian=1, Vegetarian=2) ☐

For how many days, do you eat Non Veg food in a Week? ☐

Tobacco and Alcohol Use (For the last 6 Months)

Do you smoke or Chew or Snuff tobacco? (Yes=1, No=2, Ex-smoker=3) ☐

If yes, do a Fagerstrom Test Questionnaire

Do you consume Alcohol? (Yes=1, No=2, Ex-alcoholic=3) ☐

If yes, do a Severity of Alcohol Dependence Questionnaire (SADQ)

Exercise History

Did you do any kind of exercises or sports activity in the last 6 Months? (Yes=1, No=2) ☐

If yes, how many days a week ☐

What kinds of exercise do you do

_____

Sleep Questionnaire (For the last 6 Months)

How many hours do you usually sleep (both day and night) on a working day? ☐☐

How many hours do you usually sleep (both day and night) on a Non-working day? ☐☐

(Present=1, absent=2)

Anthropometry

Height _____(cms) Weight _____(kgs)
BMI_____

Waist Circumference_____ Hip Circumference _____WHR_____

Medical History

Current Diagnosis:

Procedure Date:

Surgeon/Physician:

Summary:

Do you suffer from any other Medical Disorders?

If yes, what is the Problem
_____

Name the Medicines you
consume_____

Clinical Measures	**At Discharge**	**@ week 12**
Electrocardiographic Parameters		
Rhythm		
Qs		
ST changes		
Elevation		
Depression		
Old AWMI		
Old IWMI		
Old LWMI		
Old PWMI		
Old RVMI		
Echocardiographic Parameters		
LV EF		
LV ESV		
LV EDV		
LVEF		
LV e/e’		
LV WMSI		
LV GLS (medial)		
RSV’		

RV TAPSE		
TR grdt. Peak		
RWMA		
Metabolic Profile		
Blood Sugars- HbA1C		
Lipid Profile		
Total Cholesterol		
Serum Triglycerides		
HDL -Cholesterol		
LDL - Cholesterol		
ApoB/ApoA1		
BMI		
WHR		
Exercise Outcome Variables		
TMT Protocol		
HR achieved /THR		
Exercise duration (mins)		
METS achieved		
Duke score		
HR recovery @ 1 min (HRR)		
6 MWD (meters)		
Cardiopulmonary exercise test (CPET) variables		
VE/VCO2 Slope		
Peak VO2		
EOV		

P_{ET} CO2		
Resting		
Peak exercise		

Adverse Events During Exercise (For Groups A and C)				
Events	Baseline	During AIT	At home	At 12 weeks
Atrial Tachycardia				
VT/VF				
Syncope				
Acute MI				

Adverse Events During Exercise (For Groups B and D)			
Events	Baseline	At home	At 12 weeks
Atrial Tachycardia			
VT/VF			
Syncope			
Acute MI			

13.4 Irb Approval Letter

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Ethics Committee Registration No: ECR/326/INST/TN/2013 Re Reg-2016 Issued under Rule 122D of the Drugs & Cosmetics Rules 1945, Govt. of India

May 02, 2018

Dr Muralidar Babi,
PG Registrar,
Department of PMR,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant: New Proposal**
Effect of Aerobic Interval Training (AIT) in improving functional capacity and LV remodelling in post-MI Patients- a Randomized Controlled Trial
Dr Muralidar Babi, Employment Number: 21423P,G.Registrar, Physical Medicine and Rehabilitation, Dr George Tharion, Employment No : 30194, Dr. Oommen K George, Employment No : 13200, Dr Paul V George, Employment No : 30219, Cardiology, Dr. Viji Samuel Thomson, Employment No: 28037, Dr. Sujith Thomas Chacko, Employment No : 28278, Dr. Anoop George Alex, Employment No 32817, Cardiology , Dr Bobeena Rachel Chandy, Physical Medicine and Rehabilitation, Dr. Arun Jose Nellickal, Mrs. Mahasampath Gowri.S, Employment No: 33418, biostatistics.

Ref: IRB Min. No. 11190 (INTERVEN) dated 28.02.2018

Dear Dr Muralidar Babi,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board.

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

1 of 5

Ethics Committee Silver, Office of Research, I Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Ethics Committee Registration No: ECR/326/INST/TN/2013 Re Reg-2016 Issued under Rule 122D of the Drugs & Cosmetics Rules 1945, Govt. of India

Dr. George Thomas, M.B.B.S., D. Ortho., Ph.D.,
Chairperson, Ethics Committee

Dr. L. Jeyaseelan, M.Sc., Ph.D., FSMS, FRSS.,
Secretary, Research Committee

Prof. Keith Gomez, B.Sc., MA (S.W), M.Phil.,
Deputy Chairperson, Ethics Committee

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

May 02, 2018

Dr Muralidar Babi,
PG Registrar,
Department of PMR,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant: New Proposal**
Effect of Aerobic Interval Training (AIT) in improving functional capacity and LV remodelling in post-MI Patients- a Randomized Controlled Trial
Dr Muralidar Babi, Employment Number: 21423P,G Registrar, Physical Medicine and Rehabilitation, Dr George Tharion, Employment No : 30194, Dr. Oommen K George, Employment No : 13200, Dr Paul V George, Employment No : 30219, Cardiology, Dr. Viji Samuel Thomson, Employment No: 28037, Dr. Sujith Thomas Chacko, Employment No : 28278, Dr. Anoop George Alex, Employment No 32817, Cardiology , Dr Bobeena Rachel Chandy, Physical Medicine and Rehabilitation, Dr. Arun Jose Nellickal, Mrs. Mahasampath Gowri.S, Employment No: 33418, biostatistics.

Ref: IRB Min. No. 11190 (INTERVEN) dated 28.02.2018

Dear Dr Muralidar Babi,

The Institutional Review Board (**Silver**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Effect of Aerobic Interval Training (AIT) in improving functional capacity and LV remodelling in post-MI Patients- a Randomized Controlled Trial" on February 28, 2018.

The Committee reviewed the following documents:

1. IRB Application format
2. Patient Information sheet and Informed Consent form
3. Cvs. Of Drs. Bobeena, Anoop George, Anu Jose, George Tharion, Muralidhar Babi, Paul V George, Saujith Thomas Chacko, Viji Samuel, Oommen K George, Ms. Gowri.
4. Flow Diagram and Permission Letter.
5. No. of documents 1- 4..

The following Institutional Review Board (Silver, Research & Ethics Committee) members were present at the meeting held on February 28th 2017 at 9.45 am in the New IRB Room, Christian Medical College, Bagayam, Vellore 632002.

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Ethics Committee Silver, Office of Research, I Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788 E-mail: research@cmcvellore.ac.in

Name	Qualification	Designation	Affiliation
Dr. George Thomas	MBBS, D Ortho, PhD	Orthopaedic Surgeon, St. Isabella Hospital, Chennai, Chairperson, Ethics Committee, IRB, Chennai	External, Clinician
Rev. Dr. T. Arul Dhas	MSc, BD, DPC, PhD(Edin)	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Additional Vice Principal (Research), Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore.	Internal, Clinician
Dr. L. Jeyaseelan	MSc, PhD, FSMS, FRSS	Professor & Head, Biostatistics, Secretary (Research Committee), IRB, CMC, Vellore	Internal, Statistician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist &Epidemiologist
Prof. Keith Gomez	BSc, MA (S.W), M. Phil (Psychiatry Social Work)	Student counselor, Loyola College, Chennai, Deputy Chairperson, Ethics Committee, IRB	External, Lay Person & Social Scientist
Dr. P. Zachariah	MBBS, PhD	Retired Professor, Vellore	External, Clinician
Dr. Anuradha Bose	MBBS, DCH, MD,MRCP, FRCPCH	Professor of Paediatrics, Community Medicine, CMC, Vellore	Internal, Clinician
Dr. Sujith J Chandy	MBBS., MD., PhD., FRCP (E)	Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Dr. Ashish Goel	MBBS, MD, DM	Professor, Hepatology, CMC, Vellore	Internal, Clinician
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Suresh Devasahayam	BE, MS, PhD	Professor of Bio-Engineering, CMC, Vellore	Internal, Basic Medical Scientist

Ethics Committee Silver, Office of Research, I Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788 E-mail: research@cmcvellore.ac.in

Dr. Prasanna Samuel	MSc, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. AbhayGahukamble	MS, D Ortho, DNB(Ortho)	Associate Professor, Paediatric Orthopaedics, CMC, Vellore	Internal, Clinician
Dr. Suceena Alexander	MBBS, MD, DM	Associate Professor, Nephrology, CMC, Vellore	Internal, Clinician
Dr. Sathya Subramani	MD, PhD	Professor, Physiology, CMC, Vellore	Internal, Clinician
Dr. Shirley David	MSc, PhD	Professor, Head of Fundamentals Nursing Department, College of Nursing, CMC, Vellore	Internal, Nurse
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Mrs. IlavarasiJesudoss	MSc (N)	Professor, Head of Medical Surgical Specialty 3 and Deputy Nursing Superintendent, College of Nursing, CMC, Vellore.	Internal, Nurse

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Effect of Aerobic Interval Training (AIT) in improving functional capacity and LV remodelling in post-MI Patients- a Randomized Controlled Trial" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

IRB Min. No. 11190 (INTERVEN) dated 28.02.2018 4 of 5

Fluid Grant Allocation:

A sum of 1,00,000/- INR (Rupees One Lakh Only) will be granted for 2 years. 50,000/- INR (Rupees Fifty Thousand only) will be granted for 12 months as an Ist Installment. The rest of the 50,000/- INR (Rupees Fifty thousand only) each will be released at the end of the first year as 2 nd Installment..

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board.

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

IRB Min. No. 11190 (INTERVEN) dated 28.02.2018

Ethics Committee Silver, Office of Research, I Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 · Fax: 0416 – 2262788 E-mail: research@cmcvellore.ac.in

13.5 Dissertation Data

Sl No	stid	stid1	hosn	hosn1	name	sex	agec	age	adres	reli	educ	occu	workd	meals	tea
1	A	1	177793	D	KUMARESAN	1	16/06/1973	46	katpadi vellore	1	5	secretary	5	3	2
2	A	6	566698	H	LOGANATHAN	1	07/04/1962	57	THORAPADI	1	5	ENGINEER	6	3	4
3	C	22	142723	C	WILSON C	1	25/06/1971	48	saidapet vellore	3	5	Teacher	5	3	2
4	C	9	350001	H	RAJI	1	05/03/1981	38	Koil street, old town, vellore	1	2	Car driver	5	3	10
5	C	13	352440	H	PRAVEEN KUMAR	1	02/06/1985	34	Gandhi nagar vellore	1	5	Marketing Agent	6	3	3
6	C	6	263630	H	NEDUNCHIZIYAN	1	03/01/1962	57	Kagithapatari	1	2	Milk vendor	7	3	3
7	C	16	356995	H	GOVINDDARAJ K	1	26/07/1972	47	kumarapa Nagar	1	4	Business man	6	3	2
8	C	23	106602	D	RAJA	1	26/01/1962	57	sathuvachari vellore	1	3	business man	7	3	2
9	C	8	443539	D	JANAKIRAMAN	1	01/04/1955	64	thotapalayam	1	5	advocate	5	3	3
10	C	42	820025	B	UDAYA KUMAR	1	19/02/1963	56	periyaallapuram vellore	1	3	driver	6	3	3
11	C	38	183652	H	JAISHANKAR	1	27/05/1965	54	salavanpettai	1	6	enquiry officer	6	3	4
12	C	10	350938	H	SRINIVASAN	1	01/01/1983	37	kattupadi vellore	1	5	carpenter	5	3	3
13	C	49	833755	D	PARI	1	30/04/1975	44	ranipet vellore	1	6	veterinary doctor	5	3	3
14	C	36	456580	H	THIRUNAVAKARASU	1	16/04/1967	52	vallalar vellore	1	3	driver	5	3	3
15	C	37	532707	D	PUSHPA	2	01/01/1960	60	kalpadur vellore	1	3	home maker	7	3	4
16	C	21	241751	F	KUMAR C	1	25/10/1966	53	mullai nagar vellore	1	2	coolie	6	3	3
17	C	12	353351	H	VENKATRAMAN	1	30/11/1966	53	sathuvachari vellore	1	4	cooley	5	3	2
18	C	34	455227	H	YUVARAJ	1	11/06/1976	43	VELAPADI VELLORE	1	3	CAR DRIVER	7	3	4
19	C	7	967398	F	ANBUMANI	1	27/04/1955	64	SATHUVACHARI	1	5	RETIRED	0	3	2
20	C	29	450998	H	GAJALAKSHMI	2	08/07/1967	52	sathuvachari	1	2	home maker	7	3	1
21	C	17	156825	G	ANANDHU	1	23/08/1955	64	thotapalayam vellore	1	3	business man	5	3	8
22	C	44	457992	H	SYED KHURSHEED	1	10/03/1966	53	rn palayam vellore	2	4	business man	3	3	3
23	C	53	566273	H	MOHANDAS	1	06/05/1965	54	velapadi vellore	1	3	shopekeeper	7	3	3
24	C	47	241348	B	HEMANANDH	1	11/09/1985	34	kagithapet vellore	1	3	operator, plastic company	6	3	3
25	C	54	566933	H	SASIKUMAR	1	01/01/1975	45	katpadi sevur	1	2	labor	7	3	1
26	C	57	569336	H	VASANTHA KUMAR	1	10/08/1958	61	sathuvachari	1	3	Business	7	3	2
27	C	55	697281	A	RAMU	1	06/02/1961	59	palligonda	1	3	fireman	6	3	5
28	C	58	153283	D	SATHYAMOORTHY	1	05/02/1969	51	KOIL STREET VELLORE	1	5	Business	6	3	7
29	C	29	407423	F	DEVAPRASADAM	1	21/04/1963	56	katpadi	3	7	pastor	5	3	5
30	C	59	622192	H	RAVI	1	27/05/1964	55	chittor	1	2	business man	7	3	4
31	A	4	358211	H	KULABJHAN	1	01/01/1969	51	aulya nagar, vellore	2	3	cook	4	3	4
32	A	2	189304	H	SHANTHI	2	01/01/1973	47	vsedhuvali vellore	3	3	home maker		3	2
33	A	5	565902	H	MANI	1	14/04/1972	47	sathuvachari	1	4	business man	6	3	2
34	A	3	354642	H	ISMAIL AHMED	1	16/06/1986	33	kagithapatari vellore	2	2	auto driver	5	3	4
35	A	12	422661	H	AKEEL AHMED	1	30/05/1974	45	saidapet vellore	2	3	business man	6	3	7
36	C	2	187667	H	SARAVANAN	1	02/05/1983	36	gopalpuran vellore	1	5	lab technician	6	3	0
37	C	43	149532	F	NEELAKANDAN	1	14/06/1952	67	krishna nagar vellore	1	5	EX MLA	5	3	3
38	C	56	568342	H	SIVANANDAM	1	02/09/1977	42	vellore	1	4	business	7	3	2
39	C	48	562852	H	MOORTHI	1	01/01/1961	59	walaja	1	2	Mechanic	6	3	4
40	C	26	337751	D	GNANAMBAL	2	19/09/1967	52	thiruvalluvar street vellore	1	4	home maker	7	3	0
41	C	35	553790	D	TITUS	1	29/04/1967	52	katpadi vellore	3	3	interior designer		3	10
42	C	50	406050	G	PANEER SELVAM	1	01/01/1970	50	katpadi	1	3	painter	3	3	8
43	C	46	556275	A	KUMAR	1	27/01/1967	53	vasanthapuram vellore	3	1	sweeper	6	3	4
44	C	27	156196	F	PUSHPARAJ	1	15/01/1951	69	sathuvachari vellore	1		Retired		3	2
45	C	11	551473	A	SARAVANAN	1	01/01/1987	33	sathuvachair vellore	1	5	insurance agent	6		
46	C	52	589572	G	ANNADURAI	1	03/03/1966	54	velapadi vellore	1	2	driver	7	3	4
47	C	52	565454	H	KARUNA RAJA	1	27/10/1972	47	sathuvachari vellore	1	3	business man	7	4	4
48	C	45	791846	F	SRINIVASAN	1	12/05/1973	46	kalpudur vellore	1	5	subinspector of police	6	3	3
49	C	15	354210	H	BASKARAN	1	01/01/1966	54	shenbakkam	1	3	Tailor	6	3	3
50	C	41	815715	F	ANNAMMAL	2	01/01/1963	57	saidapet	3	2	class iv worker	6	3	5
51	C	31	454023	H	ANANTHARAMAN	1	02/02/1953	67	palavanchathu vellore	1	4	lab technician	7	3	3
52	C	33	436016	H	SARALA	2	14/04/1968	51	viuthambet	1	3	home maker	7	3	3
53	C	19	356970	H	JEGAN	1	16/09/1992	27	konavattam vellore	1	3	car driver	6	3	3
54	C	14	353941	H	THIYAGARAJAN	1	01/01/1955	65	katpadi	1	3	cooley	6	3	2
55	C	5	188703	H	GANGADHARAN	1	03/05/1960	59	katpadi	1	5	Retired		3	5
56	C	39	914962	C	RAJENDRAN	1	10/11/1961	58	katpadi vellore	1	4	business man	5	3	3
57	C	40	671985	F	RANGANATHAN VDENI	1	10/09/1963	56	street gandhi nagar	1	3	retired	3	3	6
58	C	18	357011	H	RAJA SIVLINGAM	1	22/09/1961	58	katpadi	1	4	Mechanic	6	3	1
59	C	25	984634	G	VENKATAGANAPATHY	1	05/01/1980	40	katpadi	1	3	manager hotel	7	3	2
60	C	32	523433	B	ARUL SELVAN	1	27/11/1966	53	srinivas nagar vellore	3	4	supervisor	6	3	1
61	C	3	503007		NAGARATHINAM	1	01/01/1970	50	ashok nagar	1		hospital attender	6		
62	C	4	188331	H	ARIVAZHAGAN	1	06/05/1979	40	old town vellore	1	3	autodriver	5	3	3
63	C	1111	357447	H	JAIVELU	1	08/03/1955	65	pennathur	1	2	driver	7	3	2
64	C	1	180022	H	SATHISH BABU	1	07/07/1983	36	kuppam	1	3	autodriver	5	3	3
65	C	20	357804	H	SETTU	1	01/01/1990	30	thiruvvvannamalai	1	2	farmer	6	3	

66	B	4	706248	C	MANOGARAN	1	11/03/1964	55	KOIL STREET VELLORE	1	5	ENGINEER	6	3	2
67	B	2	354308	H	ESWARA BABU	1	19/06/1961	58	walajapet	1	6	HEAD MASTER	5	3	2
68	B	1	351284	H	SARATHI	1	27/07/1989	30	ARANI	1	5	MARKETING	5	3	2
69	B	5	437930	C	DEVADOSS	1	11/03/1953	66	Melvisharam vellore	1	3	RETIRED CARPENTER		3	2
70	B	6	454644	H	GOVINDASWAMY	1	03/08/1956	63	KATPADI VELLORE	1	3	RETIRED		3	1
71	D	2	207141	B	MR KARUNAKARAN	1	02/09/1952	67	PILAYAR KOIL STREET, VELLORE	1	5	Farmer	5	3	3
72	D	1	967649	F	JAVEED BASHA	1	22/02/1975	44	SAIDAPET VELLORE	2	3	FIRE WOOD BUSINESS	6	3	12
73	D	25	454970	H	UMAPATHY	1	07/02/1971	48	THORAPADI VELLORE	1	3		7	3	3
74	D	12	450702	H	ARPUTHAM E	2	03/04/1972	47	ARNI TV MALAI	3	3	Home maker	7	3	3
75	D	21	608926	F	RAMASAMY	1	01/05/1956	63	RANIPET VELLORE	1	5	RETIRED SUB INSPECTOR	5	3	3
76	D	9	358630	H	NADARAJAN PG	1	07/06/1953	66	PERIYAALLAPURAM VELLORE	1	3	SHOP KEEPER	7	3	1
77	D	28	222847	D	RAJA KANNU	1	01/01/1952	67	KONAVATTAM VELLORE	1	3	RETIRED	0	3	2
78	D	27	457245	H	RAMAJAYAM	2	06/02/1950	69	KANGEYANALLORE VELLORE	1	3	HOME MAKER	7	3	3
79	D	14	913244	C	BALA SUBRAMANI	1	05/05/1975	44	THORAPADAVELU VELLORE	1	4	SHOP KEEPER	7	3	2
80	D	15	451451	H	SWAMY	1	16/07/1950	69	VERIPATCHIPURAM VELLORE	1	3	RETIRED	0	3	2
81	D	22	727713	B	KALAIVANI	2	09/01/1974	45	VIRUPATCHIPURAM VELLORE	3	3	HOME MAKER	7	3	1
82	D	35	562397	H	PALANI	1	27/03/1964	55	SATHUVACHARI	1	3	GENERAL STORE EXECUTIVE	7	3	6
83	D	18	358310	H	ZUBAIR AHMED	1	19/04/1972	47	MELVISHARAM VELLORE	2	4	SUPERVISOR, LEATHER FACTC	6	3	2
84	D	19	454201	H	VASUDEVAN	1	10/04/1964	55	OTTERI VELLORE	1	4	TYPIST	6	3	3
85	D	37	563180	H	DHANAPAL	1	01/01/1959	60	ALAMELURANGAPURAM VELLOF	1	2	RETIRED	0	3	3
86	D	16	451234	H	JANAKI	2	01/01/1950	69	ARIYUR VELLORE	1	3	HOME MAKER	7	3	3
87	D	13	5345	H	VIJAYA KUMAR	1	16/03/1961	58	KOSAPET VELLORE	1	6	TEACHER	5	3	2
88	D	20	233521	H	MURALI SRINIVAS	1	04/12/1970	49	GANDHI NAGAR KATPADI VELLO	1	6	ACCOUNTANT	6	3	4
89	D	39	333825	F	CITTY BABU	1	29/03/1978	41	SALVAN PET VELLORE	1	3	DAILY WAGER	6	3	3
90	D	24	454845	H	MALIGA	2	01/01/1962	58	KATPADI VELLORE	1	1	HOME MAKER	7	3	3
91	D	11	353592	H	ANUSUYA	2	01/01/1968	52	SALAVANPET VELLORE	1	3	HOME MAKER	7	3	2
92	D	38	564108	H	BALAGANESH	1	27/10/1975	44	ALLAPURAM VELLORE	1	5	GENERAL MANAGER	7	3	2
93	D	43	566785	H	NATESAN	1	01/05/1975	44	VELLORE	1	3	FARMER	7	3	1
94	D	41	564711	H	SARAVANAN	1	17/09/1970	49	KATPADI VELLORE	1	3	FARMER	4	3	4
95	D	40	949348	A	AARON SELVARAJ	1	23/12/1979	40	KOIL STREET, VELLORE	3	5	ATTENDER	6	3	4
96	D	29	457598	H	VEERA GOPAL	1	02/06/1953	66	KATPADI VELLORE	1	3	SHOP KEEPER	7	3	2
97	D	5	352002	H	RAJU	1	24/12/1977	42	GUDIYATHAM VELLORE	1	3	AUTO DRIVER	7	2	8
98	D	3	351556	H	NAGARAJAN	1	06/04/1953	66	RANGAPURAM VELLORE	1	5	RETIRED	0	3	1
99	D	23	587886		GULAB	1	25/04/1947	72	SATHUVACHARI	2	3	RETIRED	0	3	3
100	D	4	976292	A	ALBERT VEDHANAYAGA	1	02/02/1963	56	VELLORE	3	3	PASTOR	5	3	2
101	D	30	480473	H	MURUGAN	1	01/01/1975	45	ponnai vellore	1	3	farmer	6	3	5
102	D	42	566436	H	SAKTHIVEL B	1	01/01/1973	47	punniyakotti st vellore	1	2	carpenter	4	3	15
103	D	46	567579	H	SHIVAJI	1	15/06/1968	51	thorapadi vellore	1	5	engineer	4	3	2
104	D	44	566947	H	SURESH	1	03/03/1976	43	saidapet vellore	1	3	tailor	6	3	2
105	D	31	574850	D	VALAMARTHI	2	05/05/1968	51	KOSAVANPUDUR	1	3	HOME MAKER	7	3	2
106	D	47	568810	H	ARUMUGAM	1	14/03/1969	50	saidapet vellore	1	4	Technician	7	3	5
107	D	33	458907	H	BABU SHANKAR	1	28/01/1969	51	ambur vellore	1	1	daily wager	4	3	2
108	B	3	450098	H	RAMANI	2	25121	51	vellore	3	3	home maker	7	3	1
109	D	48	357661	H	SUBASH	1	23479	56	WALAJAPET	1	2	FITTER	6	3	5
110	D		995219	F	DHANASEKAR	1	22326	59	perumugai	1	5	enginner	6	3	4
111	D	6	352282	H	PICHANDI	1	18790	68	guidyatham	3	3	retired	6	3	
112	D	45	912990	F	MUSTHAQ BASHA	1	28191	43	sethuvala	2	3	business man	6	3	2
113	D	36	562975	H	NARAYANAN	1	29149	40	vellore	1	3	business	7	3	5
114	D	17	452574	H	NOOR MOHAMMED	1	23012	57	noorulah pet	2	2	retired	0	3	1
115	D	10	358797	H	ABDULLA BASHA	1	23743	55	kaspa vellore	2	4	security gurd	6	2	4
116	D	32	121655	D	SEKAR	1	21551	61	senoor post vellore	1	3	daily wager	7	3	3
117	D	26	455584	H	RAJENDRIRAN	1	21916	60	salvanpet vellore	1	2	daily wager	5	3	5
118	D	7	353149	H	SRIDHAR	1	23864	54	vilapakam	1	3	daily wager	5	3	3
119	D	34	561947	H	VENKATESAN	1	22627	58	vellore	1	2	daily wager	1	3	3

foodh	nonveg	tobac	alcoh	in	working	non	height	wet1	wet2	bmi1	bmi2	waist1	waist2	hipc1	hipc2	whr1	whr2	diab	hyper	dyslip	famhi	mitype	vessel
2	0	3	3	1	8	8	170	87	84	30.1	29.1	102	100	86	86	1.19	1.16	1	2	1	2	2	1
1	0	2	2	2	8	8	176	87.6	88.4	28.3	28.5	114	105	103	109	1.11	0.96	1	2	1	2	2	1
1	4	1	1	2	5	5	165	66.9	66.4	24.6	24.4	89	88	97	95	0.92	0.93	1	1	1	2	1	2
1	5	1	1	1	6	6	162	62.8	61	23.9	23.2	91	90	90	91	1.01	0.99	1	2	1	2	2	1
1	1	1	1	1	7	7	166	65.9	64	23.9	23.2	84	81	99	95	0.85	0.85	2	2	2	2	2	
1	2	3	3	2	7	7	165	58	59	21.3	21.7	88	89	89	89	0.99	1	2	2	2	2	2	1
1	1	2	2	1	7	7	181	83.1	81	25.4	24.7	99	95	98	99	1.01	0.96	2	1	1	2	2	1
1	1	2	2	2	8	8	165	65.5	61	24.1	22.4	89	82	94	89	0.95	0.92	2	1	2	2	1	3
1	2	2	2	1	8	8	158	61.4	59.4	24.6	23.8	87	85	94	94	0.93	0.9	1	1	2	2	2	1
1	1	2	2	2	8	8	174	85.8	83.9	28.3	27.7	101	104	106	106	0.95	0.98	1	2	1	2	1	2
2	0	2	2	1	6	6	167	86.8	81.3	31.1	29.2	109	103	108	102	1.01	1.01	1	2	1	2	2	3
1	1	2	2	2	8	8	170	66	63	22.8	21.8	84	83	93	91	0.9	0.91	2	2	2	2	2	1
1	4	2	2	1	6	6	171	73.1	71.9	25	24.6	92	92	97	93	0.95	0.99	2	2	2	2	1	1
1	1	1	1	1	7	7	165	62	61	22.8	22.4	90	91	88	89	1.02	1.02	1	1	1	2	2	1
2	0	2	2	1	8	8	150	65.8	66.5	29.2	29.6	99	92	101	105	0.98	0.88	1	1	1	2	2	2
1	1	1	1	2	7	7	155	54.2	57.7	22.6	24	81	81	87	87	0.93	0.93	1	2	1	2	1	1
1	2	2	2	2	8	8	155	62	57	25.8	23.7	88	86	90	88	0.98	0.98	1	2	1	2	2	1
1	3	1	2	1	10	10	173	82	85.2	27.4	28.5	105	108	101	104	1.04	1.04	1	2	1	2	2	4
1	2	2	1	2	8	8	165	87.7	84	32.2	30.9	102	100	104	102	0.98	0.98	2	1	1	2	1	2
2	0	2	2	2	8	8	161	68	68.2	26.2	26.3	99	95	103	107	0.96	0.89	1	1	1	2	1	4
1	2	2	1	2	9	9	171	70	64.7	23.9	22.1	97	97	83	84	1.17	1.15	1	1	1	2	2	2
1	2	2	2	2	7	7	165	63.9	63.1	23.5	23.2	87	92	93	91	0.94	1.01	1	1	2	2	2	1
1	1	2	2	2	8	8	171	66.5	67.1	22.7	22.9	94	91	93	94	1.01	0.97	1	2	1	2	1	2
2	0	1	2	2	8	8	170	107.6	104.2	37.2	36.1	121	119	118	115	1.03	1.03	2	2	1	2	2	1
1	1	2	2	2	7	7	166	67.3	65.4	24.4	23.7	92	90	87	89	1.06	1.01	1	2	1	2	2	2
1	2	2	2	1	7	8	165	63.2	60.9	23.2	22.4	91	92	96	89	0.95	1.03	1	1	1	2	2	3
1	2	2	2	2	9	11	166	67.5	65.9	24.5	23.9	92	94	104	96	0.88	0.98	2	2	2	2	2	2
1	3	1	1	2	6	6	159	69.8	63.8	27.6	25.2	97	88	98	91	0.99	0.97	2	1	1	2	2	1
1	1	2	2	2	8	8	170	69	69.1	23.9	23.9	101	99	96	94	1.05	1.05	1	1	2	2	1	1
2	1	1	2	1	7	7	169	64.8	67.4	22.7	23.6	73	90	74	91	0.99	0.99	1	2	2	2	2	4
1	1	3	2	2	8	8	162	47.1		17.9		77		86		0.9		2	1	2	2	2	1
1	3	2	2	2	6	6	159	80.3		31.8		101		114		0.89		2	1	1	2	2	1
1	2	2	2	2	8		171	71.5		24.5		98		90		1.09		1	1	1	2	2	2
1	1	1	2	2	6	11	172	76		25.7		94		97		0.97			2	1	2	2	1
1	2	3	2	2	7	7												2	2	1	2	1	2
1	4	1	1	2	6	7	166	81.4		29.5		98		108		0.91		2	2	1	2	2	1
1	2	2	2	1			161	88		33.9		88			87			1	2	2	2	1	2
1	1	2	2	2	7	8	156	61.9		25.4		84		92		0.91		2	2	1	2	2	1
1	1	2	2	2	7	8	167	67.3		24.1		98		96		1.02		2	1	2	2	2	2
1	1	2	2	2	7	7	156	67		27.5		88		112		0.79		1	1	1	2	2	3
1	4	1	1	2	8	8	170	67.3		23.3		91		94		0.97		1	1	1	2	2	1
1	1	3	1	2	7	7	176	82.2		26.5		100		103		0.97		2	2	1	2	2	1
1	2	1	2	2	8	8	167	52		18.6		87		86		1.01		1	2	1	2	2	1
1	1	2	2	2	7	7	170	64		22.1		89		93		0.96		1	1	1	2	1	1
1																		2	2	1	2	2	1
1	1	3	3	2	7	7	166	66.4		24.1		92		94		0.98		1	2	1	2	2	4
1	5	1	1	1	7	7	171	75		25.6		103		96				1	2	1	2	2	2
1	1	1	3	2	7	8	180	81.6		25.2		101		101		1		2	2	2	2	1	1
1	0	1	2	2	8	8	174	66.3		21.9								2	2	1	2	2	1
1	2	2	2	2	8	8	154	76		32		107		110		0.97		2	1	2	2	2	2
1	1	2	2	2	7	7	176	79		25.5		100		104				1	2	1	2	2	2
1	2	2	2	1	8	8	156	63.4		26.1		96		106				1	2	1	2		4
1	7	1	1	2	10	10	172	71.7		24.2		90		94				2	2	2	2	2	1
1	1	2	2	2	8	8	171	82										2	2	2	2	2	1
1	1	1	2	1	7	8	175	84		27.4		106		104		1.02		1	2	1	2	2	2
1	2	2	1	1	6	6	171	88.4		30.2		114		111				1	1	1	2	2	4
1	1	1	2	2	7	7	161	60.5		23.3		88		92		0.96		1	2	1	2	2	2
1	1	2	2	2	7	7	169	71.2		24.9		91		98		0.93		1	2	1	2	2	1
1	1	1	2	2	4	4	170	69		23.9		93		91				2	2	1	2	2	3
1	1	1	2	2	7	8	165	54		19.8		87		87		1		2	1	2	2	1	1
																		1	1	1	2	2	2
1	1	1	1	2	9	9	165	88		32.3		106		105		1.01		1	1	1	2	2	1
1	1	2	2	2	6	6	166	68		24.7								1	1	1	2	1	2
1	3	1	3	2	8	8	172	85.1		28.8		101		104		0.97		1	2	1	2	2	1
1	1	1	2	2			177	53		16.9		80		73				2	2	1	2	1	1

treatm	lvef1	lvef2	lvesv1	lvesv2	lvedv1	lvedv2	lve1	lve2	lvw1	lvw2	lvg1	lvg2	rvs1	rvs2	rvt1	rvt2	trg1	trg2	rw1	rw2
1	36.9	59.3	35.2	31.6	55.8	77.6	13	10.6	1.47	1.11	14.1	17.2	9.84	10.3	16.8	21.7	6.85	15.6	1	1
1	40.4	48	45	28.9	75.5	55.5	15.4	15.2	1.47	1.23	12	12.8	12.2	9.74	15.8	15.4	8.44	25.5	1	1
1	60.1	62.6	27.5	21.6	69	57.8	9.14	8.29	1	1	13.9	17.4	10.5	9.32	18	23.8	16.2	6.71	2	2
1	59.2	65.2	24.6	21	60.3	60.5	8.69	8.2	1	1	18.3	20.2	10.6	11.1	21.7	21.7	10.9	7.7	2	2
3	57	60.9	19.4	32.7	45.1	83.6	9.11	7.81	1.2	1	17.5	18.7	11.6	11	22.7	29	12.7	14.8	1	2
1	57.8	54.8	28.2	19.4	66.9	42.9	11.1	8.55	1.11	1	17.6	14.3	10.2	10.7	19	19.1	9.54	11.8	1	1
1	52.4	59.3	30.1	37.9	63.3	93.1	11.4	9.55	1	1	18.2	22.5	10.3	12.5	17	23.6	10.5	8.59	2	2
1	65.2	66	18.7	20.7	50.8	60.9	11.3	14.1	1	1	15.5	20.6	11.6	12.7	21.7	25.8	14.2	9.54	2	2
1	54.5	62.4	33.6	31.4	73.9	83.5	16.6	15.3	1.17	1	15.6	18.3	9	10.8	20	19.3	16.7	14	1	2
1	59.7	58.5	16.9	17.1	41.9	41.1	13.5	12	1	1	16.7	15.9	15.1	11.9	23.1	19.7	14.4	14	2	2
1	49.8	57.2	20	17	39.9	39.8	10.8	10	1.23	1	14.7	17.2	12.51	10.9	22.7	21.4	18.9	11.9	1	2
1	55.6	57.2	45.6	37.1	103	86.6	9.22	9.2	1.29	1.23	15.6	17.8	11.3	11.8	18.9	25.8	9.86	22.7	1	1
1	57.2	63.4	33.7	25.1	78.7	68.5	6.92	9.26	1.17	1	17.3	19.5	12.8	12.1	19.4	21.7	7.27	12.1	1	1
1	64.4	66.9	31.3	17.3	87.9	52.4	8.05	12.8	1	1	18.4	19.6	10.3	10.6	19.7	25.5	7.41	8.59	2	2
1	47.5	48.7	59.2	45.3	113	91.8	8.41	9.55	1.88	1.41	8.3	9.6	12.4	11.2	21.2	19	12.9	6.85	1	1
1	50	60	39.1	24.9	78.2	62.2	8.14	11	1.11	1	17.7	18.6	8.58	10.2	14.9	24.6	3.65	4.83	1	2
1	44.6	58.9	24.8	35.7	44.7	85.3	12.6	8.48	1.35	1.17	12.2	15.6	11.5	9.84	15.9	14.9	14.8	16.9	1	1
2	60.3	64.8	34.9	23.4	88	66.4	11.5	8.6	1	1	15.2	14.1	11	12.6	21	23.8	7.22	6.44	1	2
1	57.6	64.3	22.6	18.4	53.4	51.5	15.7	12.7	1	1	21.8	22.5	10.5	14.1	21.9	25.5	7.99	13.8	2	2
3	60	61.2	20.6	22.5	51.1	58.1	9.24	12.7	1	1	17.8	17.4	8.27	9.84	20.9	20.2	10.2	11.6	2	2
1	40.8	58	41	20.1	69.4	47.9	14.6	9.99	1.88	1.11	9	15.1	12.4	15.2	20.2	20	8.59	8.29	1	1
1	64.4	65.7	21.4	21.5	60.2	62.7	12.4	14.5	1	1	20	18.6	13.2	14.4	22.2	25.5	10.9	12.9	2	2
1	44.4	47.2	45.7	50.1	82.1	94.9	17.9	18.7	1.42	1.88	10.5	15.5	8.58	11.6	15.1	19.9	24.7	16.9	1	1
1	49.8	60.9	33	34.1	65.7	87.1	8.31	11.9	1.29	1	11.3	15.4	5.97	9.42	10.8	17.8			1	2
1	54.6	63.7	24.4	16.3	53.8	44.9	8.26	9.17	1.29	1	11.9	20.9	11.7	9.63	22.6	27.9	7.41	13.8	1	2
1	62.7	65.1	14.9	19.7	39.9	56.4	9.77	14	1	1	17.5	19.9	13.9	13.6	25.5	23.4	12.7	10.4	2	2
1	42.2	62.5	36	19.3	62.3	49.9	18.1	16.5	1.41	1	14.8	15.9	12.4	13.4	16.4	26.5	8.75	21.9	1	2
1	59.6	62.3	13.2	15	32.6	39.7	12.6	9.23	1	1	15.3	20.5	12.2	11.6	23	19.1	5.43	11.9	2	2
1	38.4	46.1	46.8	33.5	75.2	62.1	18.1	23.6	1.1	1.29	11	15.2	6.28	6.28	12.2	15.4	9.13	7.13	1	1
1	38.9	55.4	46.4	33	75.8	74.1	11.2	6.84	1.7	1.05	10.9	14.4	13	13.3	22.2	21	14.8	4.06	1	1
1	39.4	48.2	63.9	51.1	105	98.4	8.56	12.3	1.41	1.23	11.1	13.3	10.7	10.5	15.3	15.9	5.43	9.22	1	1
1	40.6	38.9	49.7	41.7	83.7	68.4	8.96	10.9	1.47	1.64	13.5	14.2	9.63	11.9	17.8	17.8	10.4	7.27	1	1
1	31.8	34.9	45.5	63.1	66.7	96.9	23.1	29.6	1.74		10.6	11.3	9.84	9.94	14.9	16.1	25.2	46.3	1	1
1	58.9	62.4	25.9	19.6	63	52	8.69	12	1	1	17.1	20.5	10.3	14.9	26	26.9	10.2	14	2	2
1	63.1	55.7	21.9	19.5	59.4	43.9	7.92	6.8	1	1.17	21.4	19.4	9.42	9.42	21.3	18.7	9.38	11.6	2	1
1	59.7	63.2	20	20.4	49.6	55.5	9.44	10.2	1.05	1	20.3	20.2	9.32	10.8	18.7	20.8	6.44	13.6	1	2
1	47.7	61.7	39.8	17.5	76.1	45.6	16.7	15.5	1.35	1	12.2	20.3	9.9	9.21	17	20	11.8	4.95	1	2
3	43.6	53.7	33.2	22.9	59	49.6	10.6	10.5	1.47	1.29	11.3	14.8	8.48	7.22	20.7	13.2	5.67	7.99	1	1
1	58.5	50.2	37.1	35.3	89.4	70.8	12.7	10.5	1	1.29	14.4	16.6	11.6	11.3	18	20.7	15.8	16	2	1
1	58.9	61.3	24.1	19.5	58.7	50.5	13.2	14.1	1.21	1.12	18.8	19.2	13.1	11	21.7	17.8	25.5	15	1	1
1	48.4	57.3	20.6	17.4	39.9	40	14.3	15.3	1.23	1	14.5	16.6	10.9	10.8	18.3	18.5	12.9	9.7	1	2
1	56.2	48.3	18.3	31.5	41.9	61.1	11.4	10.3	1	1.29	16	15.2	10.4	12.8	19	19.3	8.92	11	2	1
1	42	47	28.6	27	52	50.9	14.6	17.6	1	1.29	11.1	13.3		9.21	12	12	10	10.7	1	1
1	56.2	68.1	21.5	17.5	49.2	54.8	11	10.8	1.25	1	15.5	18.6	13.5	12.7	18.3	27.2	13	9.54	1	2
1	57.9	63.5	25	17.4	59.5	47.5	7.95	7.87	1	1	18.8	19.9	10.8	13	19.9	24.2	10.2	7.41	2	2
1	50.2	41.7	48	53	98	91	13.9	16.4	1.23	1.35	11	12.1	11.6	9.11	21.4	19.9	7.84	12.1	1	1
1	64.6	65.2	23.5	21.4	66.4	61.4	9.14	11.2	1	1	18.2	20.1	11.2	12.7	19.1	21.2	17.1	8.29	2	2
1	55.6	59.6	28.5	22.2	64.1	54.9	13.3	15	1	1	14.4	15.1	11.4	12.5	19.9	23.4	10.9	12.5	1	1
1	54.7	53.2	18.3	19.6	40.4	41.9	28.9	21.6	1.23	1.23		17.5	9.63	9.74	22	14.9	11.6	15	1	1
1	56.3	62	25.8	21.2	59	55.7	11.5	11.5	1	1	16.2	17.7	12.2	10.7	24.8	21.4	25.6	14.8	2	2
3	63	62	26	27.3	70.3	71.9	15.9	10.1	1	1	18.1	18	10.6	15.2	21.4	20.2	7.41	7.55	1	2
1	44.2	33.6	31.2	58.5	55.9	88.1	26.1	20.5	1.47	2.47	10.7	9.8	8.48	9.21	15.3	10.8	4.27	26.9	1	1
2	51.6	56.1	25.7	23.6	53	53.9	17.9	11.8	1	1.1	12.6	14.8	10.4	10	17.8	15.7	5.8	5.92	1	1
1	43.7	44.1	53.7	54.2	95.5	96.9	15.3	14	1.11	1.23	6.3	10.5	10.6	12.5	18.8	19.3	15.8	10.2	1	1
1	56.5	64.4	23.7	15.5	54.5	43.4	9.36	9.88	1.17	1	17.5	16.3	10.6	12	16.4	22.4	4.38	4.17	1	2
1	55.7	60.5	23.4	20.8	52.7	52.7	8.34	8.66	1.41	1	15.1	16.3	12.8	11.7	17.4	23.6	13.4	6.85	1	2
1	63	63.6	31.6	28.5	85.6	78.2	10.4	9.78	1	1	20.4	17	13.2	12.8	24.9	23.8	10.7	9.86	2	2
1	60.7	62.5	15.8	12	40.2	32	9.35	8.71	1	1	17.6	21.2	11.3	9.84	17	18.3	13.8	12.9	2	2
1	43.5	53.4	24.9	23.6	44.1	50.6	11.8	15.5	1.23	1	15.3	16.7	9.84	12	14.4	19.7	8.29	5.18	1	1
1	60.6	64.7	29.3	26.5	74.3	75	8.53	8.33	1	1	18.4	17.9	12.8	11.6	22.5	19.7	16.2	15.6	2	2
1	50.2	52.3	45.1	34.5	90.5	72.2	10.8	10.4	1.11	1.35	12.8	15.3	15.8	9.32	25.5	24.1	12.5	12.3	1	1

rwm1	rwm2	hba1	hba2	tc1	tc2
whole anterior, anteroseptum, anterolateral, apex	basal and mid infero septum	6.5	6.1	173	109
whole anteroseptum, anterior, apical septum	mid and apical anterior, anterio septum hypokinetic	11.2	8.2	172	94
		5.6	6	204	203
na	na	7.6	6.6	201	108
Mid anteroseptum, apical septum, apex,mid anterior	Nil		4.6	142	117
Basal infero septum	basal posterolateral hypokinetic	6.4	6.2	129	109
Nil	Nil	6	5.9	202	122
na	na	5.1	5.1	181	91
basaland mid infero septum, basal inferior	na	8.1	7.3	131	95
na	na	7.4	7.7	142	134
basal and mid inferior,mid anteroseptum infero septum	na	9	6.3	207	111
mid anterior septum,anterolateral , inferoseptum, apex	basal and mid antero septum, mid infero septum, apical anter	5.5	5.3	149	113
mid anteroseptum, apical septum apical anterior	apical anterior, antero septal	5.3	5.4	182	103
na	na	8.7	6.9	140	112
all segments except septal and inferior are hypokinetic	mid and apical anterior , antero septum, basal inferior, api	7.9	8.7	106	97
basal inferior, inferoseptum hypokinetic	na	7	6.8	171	92
mid antero septum, anterolateral and mid apical anterior ape	apical ant,septum, mid anteorlateral	6.1	5.6	200	129
basal inferior hypokinetic	na	11.7	11	168	104
na	na	5.8	5.6	205	124
na	na	5.9	5.9	261	152
basal and mid anteroseptum, anterior apical,apical anterior,	basal anteroseptum, apical anterolateral	9.9	5.7	163	74
na	na	7.5	7.7	129	88
whole inferolateral, inferior, basal,mid anterorlateral	entire inferolateral,mid and apical inferior	10.3	6.3	185	132
basal and mid posterorlateral, whole inferiror wall,rv dysfu	NA	5.8	5.9	151	81
Basal and mid anteroseptum, anterior and apex hypokinetic	NA	12	11.5	233	114
na	na	8	7	217	117
whole inferior septum, inferior and infirolateral wall	na	6.4	6.5	100	119
na	na	5.7	5.2	240	115
mid inferoseptum hypokinetic	NA	6.2	7.3	138	117
na	na	7.6	7.6	121	92
Mid anteroseptum, apical septum, midanterolateral, apical in		5.5		159	
Mid anterior septum, whole inferior septum, apex		6.1		151	

ANTERIOR, ANTEROSEPTAL, APICAL, APEX	WHOLE ANTEROSEPTUM,APICAL SEPTUM, ANTERIOR AND APEX	7.7	7.8	135	99
MID ANTEROSEPTAL, BASAL-MID ANTERIOR, APICAL, INFEROSEP,APE	MID ANTEROSEPTUM , HYPOKINETIC	11.8	7.1	161	116
ANTEROSEPTUM, ANTERIOR INFERO SEPTUM,	BASAL AND MID ANTERIOR SEPTUM	11	6.5	127	87
WHOLE INFEROSEPTUM, BASAL AND MID INFERIOR BASAL AND MID	ENTIRE ANTEROSEPTUM, INFEROSEPTUM, INFERO APICAL	8	8	97	133
WHOLE ANTEROSPETUM, ANTERIOR, ANTEROLATERAL, MID,APICAL,A	ANTEROSEPTUM, ANTERO LATERAL AND APEX	5.9	5.7	272	114
NIL	NIL	5.6	5.6	168	183
NIL	MID INFEROSEPTUM ,BASAL, MID INFERIOR	5.5	5.7	269	167
MID ANTERO SEPTUM HYPOKINETIC	NIL	6.2	6.1	198	114
APICAL ANTERIOR, BASAL AND MID ANTERO SEPTUM, INFERO SEPTU	NIL	12	9.5	256	236
INFEROSEPTUM, BASAL INFERIOR	BASAL,MID ANTEROSEPTUM, ANTERIOR BASAL INFERO SEPTUM	8.6	6.5	141	133
NIL	BASAL AND MID ANTEROLATERAL, INFERO LATERAL APICAL LATERAL	6.1	6	217	141
BASAL MID POSTEROLATERAL MILDLY	BASAL POSTEROLATER AND MID ANTEROLATERAL	14	8	200	169
BASAL ANETROSEPTUM,ANTERIOR, ANTERO LATERAL AND MID ANTE	NIL	6	6.4	238	110
NIL	MID ANTEROSEPTUM, MID AND APICAL ANTERIOR,APICAL LATERAL A	5.8	6	184	116
BASAL MID INFEROSEPTAL	BASAL AND MID INFEROLATERAL INFERIOR AND BASAL INFEROSEPTU	5.8	5.4	163	102
MID ANTERIOSEPTUM , APICAL ANTERIOR, APICALSEPTUM	NIL	10.1	6.7	204	104
NIL	NIL	8.3	8.7	137	85
WHOLE ANTEROSEPTUM, APEX, APICAL ANTERIROR	BASAL AND MID ANTEOR SEPTUM, MID AND APICAL ANTERIROR	5.9	5.7	192	119
NIL	NIL	10.8	8.6	223	149
ANTERIOR MILDLY HYPOKINETIC	ANTERO SEPTUM MILDLY HYPOKINETIC	6.3	6.4	199	121
BASAL,MID ANTEROLATERAL, MID INFEROLATERAL, MID ANTERIOR	BASAL AND MID ANTERORLATERAL, ANTERIOR	9.2	6.3	215	139
NIL	NIL	7.4	6.2	226	136
APICAL ANTERIOR MILD HYPOKINETIC	NIL	7.2	7.5	187	103
WHOLE ANTERIOR, ANTEROLATERAL, MID AND APICAL, ANTERO SEPT	BASAL AND MID ANTEROSEPTUM, ANTERIOR, ANTERIOLATERAL, APIC	10.5	6.5	196	167
basal inferior, infero septum	basal inferosteptum	9.8	8.2	199	106
WHOLE ANTEROSEPTUM, INFERO SEPTUM, INFERIOR WALL	WHOLE ANTERO SEPTUM, BASAL AND MID INFEROSEPTUM	10.3	9	185	111
BASAL AND MID INFEROSEPTUM INFERIOR	NA	6	6.6	253	227
MID and APICAL, LATERAL, ANTERIOR AND APEX	NA	10.4	8.6	167	76
NA	NA	8.7	8.1	211	107
NA	NA	5.7	6	205	104
WHOLE ANTERO SEPTUM, BASAL AND MID ANTERIOR HYPOKINETIC	BASAL ANTERIOR, HIGHLY HYPOKINETIC	8.9	6.5	198	112
NA	NA	6	6.2	209	135
ANTERIOR, ANTERO SEPTUM	WHOLE ANTERIOR SEPTUM ANTEROIOR WALL	5.4	5.6	132	82

tg1	tg2	hdl1	hdl2	ldl	ld2	th1	th2	nh1	nh2	pekh1	pekh2	dur1	durm1	durs1	netd1	dur2	durm2
114	79	25	23	145	67	6.92	4.74	148	86	85	91	6.21	6	21	6.35	10.04	10
167	80	35	30	111	54	4.91	3.13	137	64	75	77	1.07	1	7	1.12	5.1	5
320	389	33	37	123	120	6.18	5.49	171	166	68	78	7.16	7	16	7.27	9.08	9
359	151	51	42	125	45	3.94	2.57	150	66	69	82	10.17	10	17	10.28	12.44	12
163	205	41	31	98	62	3.46	3.77	101	86	87	96	11.18	11	18	11.3	14	14
84	65	27	36	91	62	4.78	3.03	102	73	76	92	8.1	8	10	8.17	10.01	10
337	226	35	34	153	86	5.77	3.59	167	88	87	98	7.55	7	55	7.92	13.01	13
72	72	34	39	114	42	5.32	2.33	147	52	89	107	6.24	6	24	6.4	10.05	10
88	87	27	25	108	60	4.85	3.8	104	70	84	104	6.15	6	15	6.25	9.18	9
96	125	26	24	114	89	5.46	5.58	116	110	78	87	5.27	5	27	5.45	8.12	8
140	119	47	41	144	55	4.4	2.71	160	70	86	87	4.15	4	15	4.25	8.55	8
60	153	42	35	106	46	3.55	3.23	107	78	80	83	10	10	0	10	12.07	12
76	118	42	32	140	57	4.33	3.22	140	71	93	97	9.34	9	34	9.57	13.19	13
299	286	27	29	81	52	5.19	3.86	113	83	76	80	6.53	6	53	6.88	11.09	11
72	85	40	38	51	41	2.65	2.55	66	59	84	80	2.2	2	20	2.33	4.02	4
290	79	36	36	111	45	4.75	2.56	135	56	72	79	8.23	8	23	8.38	7.14	7
113	105	40	39	155	85	5	3.31	160	90	83	88	4.19	4	19	4.32	10.02	10
255	83	29	34	114	61	5.79	3.06	139	70	95	93	5.21	5	21	5.35	9.03	9
187	118	32	28	145	77	6.41	4.43	173	96	77	90	7.12	7	12	7.2	9.27	9
136	93	44	40	169	106	5.93	3.8	217	112	100	102	3.5	3	50	3.83	8	8
315	147	32	25	94	37	5.09	2.96	131	49	83	92	5.29	5	29	5.48	7.48	7
68	77	42	36	80	42	3.07	2.44	87	52	79	101	6.27	6	27	6.45	12.01	12
116	99	36	33	135	87	5.14	4	149	99	83	93	4.14	4	14	4.23	11.03	11
96	91	39	29	116	44	3.87	2.79	112	52	67	87	1.38	1	38	1.63	8.13	8
286	138	34	30	157	69	6.85	3.8	199	84	73	89	5.42	5	42	5.7	10.1	10
265	134	34	33	158	61	6.38	3.55	183	84	64	87	6.14	6	14	6.23	8.3	8
70	106	29	34	60	64	3.45	3.5	71	85	69	87	2.39	2	39	2.65	9.27	9
225	78	51	38	165	65	4.71	3.03	189	77	85	89		9	53	9.88		10
128	54	34	47	90	67	4.06	2.49	104		84	92		6	23	6.38		7
80	81	27	30	86	55	4.48	3.07	94	62	90	88		5	27	5.45		9
106		35		118		4.54				73			6	9	6.15		
195		52		93						78			3	11	3.18		
88	80	35	37	94	60	3.86	2.68	100	62	77	86	6.43	6	43	6.72	7.56	7
57	60	52	54	111	56	3.1	2.15	109	62	88	105	4.37	4	37	4.62	7.56	7
219	141	30	27	80	37	4.23	3.22	97	60	70	87	4.32	4	32	4.53	7.51	7
140	236	20	33	58	85	4.85	4.03	77	100	95	110	4.57	4	57	4.95	7.12	7
243	102	38	35	215	69	7.16	3.26	234	79	86	78	3.41	3	41	3.68	4.01	4
138	101	43	41	120	87	3.91	4.46	125	142	74	92	7.22	7	22	7.37	9.5	9
243	309	34	36	223	99	7.91	4.64	235	131	74	83	9.13	9	13	9.22	9.14	9
222	135	34	33	135	64	5.82	3.45	164	81	61	65	7.45	7	45	7.75	7.23	7
332	469	42	44	135	141	6.1	5.36	214	192	54	60	2.28	2	28	2.47	3.05	3
182	127	21	25	107	93	6.71	5.32	120	108	83	82	6.09	6	9	6.15	3.18	3
135	98	31	36	169	110	7	3.92	186	105	63	94	8.42	8	42	8.7	7.31	7
165	151	42	40	133	107	4.76	4.22	158	129	75	85	5.32	5	32	5.53	6.14	6
75	72	58	39	211	53	4.1	2.82	180	71	77	83	6.05	6	5	6.08	5.5	5
112	49	32	31	137	68	5.75	3.74	152	85	69	86	1.21	1	21	1.35	5.08	5
65	46	30	27	130	58	5.43	3.78	133	75	85	85	3.45	3	45	3.75	5.17	5
174	76	36	34	163	65	5.67	3.06	168	70	78	91	7.52	7	52	7.87	9.27	9
107	87	24	22	107	63	5.71	3.86	113	63	65	75	2.1	2	10	2.17	4.35	4
135	76	37	36	143	86	5.19	3.31	155	83	84	91	3.13	3	13	3.22	3.57	3
309	193	43	37	140	83	5.19	4.03	180	112	82	96	7.14	7	14	7.23	9.2	9
286	147	43	40	145	64	4.63	3.02	156	81	89		3.18	3	18	3.3		
88	121	41	39	135	70	5.24	3.56	174	100	85	91	3.31	3	31	3.52	4.11	4
114	132	30	29	188	97	7.53	4.69	196	107	86	92	4.07	4	7	4.12	4.33	4
179	120	34	28	135	68	5.5	3.68	153	75	78	87	6.23	6	23	6.38	6.2	6
205	125	32	42	155	112	6.13	3.98	164	125	83	71	1.41	1	41	1.68	1.57	1
196	114	41	35	143	60	4.85	3.03	158	71	92	99	6.21	6	12	6.2	3.45	3
203	98	34	34	146	65	5.44	3.26	151	77		73					1.51	
407	274	30	34	159	150	8.43	6.68	223	193	74	99	8.13	8	13	8.22	10	10
449	179	23	18	93	31	7.26	4.22	144	58	68	94	6.12	6	12	6.2	10.55	10
224	199	32	27	161	60	6.59	3.96	179	80	74	92	7.48	7	48	7.8	9.24	9
209	148	40	35	135	50	5.13	2.97	165	69	92	74	7.56	7	56	7.93	7.13	7
81	88	47	32	140	70	4.21	3.5	151	80	76	88	1.42	1	42	1.7	4.19	4
52	84	50	39	150	76	4.18	3.46	159	96	85	99	8.34	8	34	8.57	9.23	9
118	73	30	33	100		4.4	2.48	102	49	80	78	3.4	3	40	3.67	3.44	3

1	NOT WILLING TO COME	1	
1	NOT WILLING TO COME	1	2
1	NOT WILLING TO COME	1	2
1	NOT WILLING TO COME	3	2
1	JOINED WORK	3	2
1	JOINED WORK	3	2
1	JOINED WORK	2	2
1	SOCIAL REASONS	2	2
1	JOINED WORK	2	2
1	LOWER LIMB FRACTURE	2	2
1	THIGH HERPEZ ZOSTER	2	1 CA OVERY
1	NOT WILLING TO COME	2	1 NON COOPERATIVE
1	JOINED WORK	2	1 NON COOPERATIVE
1	JOINED WORK	2	1 NON COOPERATIVE
1	NOT WILLING TO COME	2	1 NON COOPERATIVE
1	JOINED WORK	2	1 NON COOPERATIVE
1	KNEE PAIN	1	1 NON COOPERATIVE
1	NOT WILLING TO COME	1	1 NON COOPERATIVE
1	JOINED WORK	1	1 NON COOPERATIVE
1	NOT WILLING TO COME	1	1 NON COOPERATIVE
1	REINFARCT, NO MONEY	1	1 NON COOPERATIVE
1	NOT WILLING TO COME	1	1 NON COOPERATIVE
1	NOT WILLING TO COME	1	1 NON COOPERATIVE
1	CHOLILITHIASIS	1	
1	NOT WILLING TO COME	1	
1	JOINED WORK	1	
1	NOT WILLING TO COME	1	
1	JOINED WORK	1	
1	NOT WILLING TO COME	1	
1	JOINED WORK	1	
1	KNEE PAIN	1	
1	NOT WILLING TO COME	1	
1	NOT WILLING TO COME	1	