# EVALUATION OF SYSTOLIC TIME INTERVALS AND HEART RATE VARIABILITY AS INDICATORS OF CARDIAC AUTONOMIC FUNCTION AMONG MALE ISCHEMIC HEART DISEASE PATIENTS

Thesis Submitted

To

**SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH**

**For the requirement of the degree**

**DOCTOR OF PHILOSOPHY IN PHYSIOLOGY**

**Under**

**Faculty of Medicine**

By

**Miss. Smitha P S, M.Sc. (Medical Physiology)**

**Under the guidance of**

**Dr. Vinutha Shankar M S**

**Department of Physiology**

**Sri Devaraj Urs Medical College, Constituent Institute of**

**Sri Devaraj Urs Academy of Higher Education and Research**

**Tamaka, Kolar, Karnataka, INDIA**

**JANUARY 2023**

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# ABBREVIATIONS

| | | |
|---|---|---|
| 1. | **STI** | Systolic Time Intervals |
| 2. | **HRV** | Heart rate variability |
| 3. | **IHD** | Ischemic Heart disease |
| 4. | **ACS** | Acute coronary syndrome |
| 5. | **IEC** | Institutional Ethical Committee |
| 6. | **MI** | Myocardial Infarction |
| 7. | **LVEF** | Left Ventricular Ejection Fraction |
| 8. | **PEP** | Pre-Ejection Period |
| 9. | **LVET** | Left Ventricular Ejection Time |
| 10. | **$QS_2$** | Total electro-mechanical systole |
| 11. | **ACE** | Angiotensin Converting Enzyme |
| 12. | **RWMA** | Regional Wall Motion Abnormality |
| 13. | **CVD** | Cardio Vascular Disease |
| 14. | **S/P PCI** | Status Post Percutaneous Coronary Intervention |
| 15. | **LVSD** | Left Ventricular Systolic Dysfunction |
| 16. | **LVDD** | Left Ventricular Diastolic Dysfunction |

# DECLARATION BY THE CANDIDATE

I, **Miss. Smitha P S,** hereby declare that this thesis titled **"Evaluation of Systolic Time Intervals and Heart Rate Variability as indicators of Cardiac Autonomic Function among male Ischemic Heart Disease patients"** is an original research work carried out by me for the award of **Doctor of Philosophy** in the subject of **Physiology (Faculty of Medicine).**

This study was carried out under the Supervision of **Dr. Vinutha Shankar M S,** Professor and Head, Department of Physiology, Sri Devaraj Urs Medical College, a Constituent Institute of Sri Devaraj Urs Academy of Higher Education and Research and under the Co-supervision of **Dr. Raveesha A,** Professor and Head, Department of General Medicine, Sri Devaraj Urs Medical College. No part of this has formed the basis for the award for any degree of fellowship previously elsewhere.

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# DECLARATION BY THE GUIDE

This is to certify that the original research work contained in the thesis titled **"Evaluation of Systolic Time Intervals and Heart Rate Variability as indicators of Cardiac Autonomic Function among male Ischemic Heart Disease patients"** in the subject of Physiology was carried out by **Miss. Smitha P S** (Reg. No.19PY1002) for the requirement of the award of Doctor of Philosophy under the Faculty of Medicine.

This study was carried out under the guidance of Dr. Vinutha Shankar MS, Professor, and Head of the Department of Physiology, Sri Devaraj Urs Medical College, a Constituent Institute of Sri Devaraj Urs Academy of Higher Education and Research.

Any part of this thesis is not been submitted elsewhere for the award of any degree of fellowship previously.

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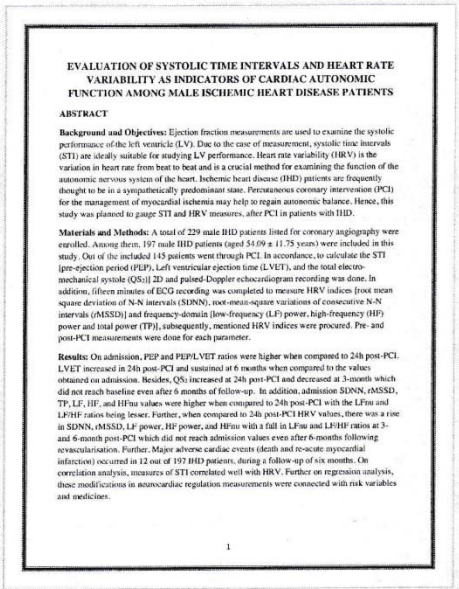

**EVALUATION OF SYSTOLIC TIME INTERVALS AND HEART RATE VARIABILITY AS INDICATORS OF CARDIAC AUTONOMIC FUNCTION AMONG MALE ISCHEMIC HEART DISEASE PATIENTS**

**ABSTRACT**

**Background and Objectives:** Ejection fraction measurements are used to examine the systolic performance of the left ventricle (LV). Due to the ease of measurement, systolic time intervals (STI) are ideally suitable for studying LV performance. Heart rate variability (HRV) is the variation in heart rate from beat to beat and is a crucial method for examining the function of the autonomic nervous system of the heart. Ischemic heart disease (IHD) patients are frequently thought to be in a sympathetically predominant state. Percutaneous coronary intervention (PCI) for the management of myocardial ischemia may help to regain autonomic balance. Hence, this study was planned to gauge STI and HRV measures, after PCI in patients with IHD.

**Materials and Methods:** A total of 229 male IHD patients listed for coronary angiography were enrolled. Among them, 197 male IHD patients (aged 54.09 ± 11.75 years) were included in this study. Out of the included 145 patients went through PCI. In accordance, to calculate the STI [pre-ejection period (PEP), Left ventricular ejection time (LVET), and the total electro-mechanical systole ($QS_2$)] 2D and pulsed-Doppler echocardiogram recording was done. In addition, fifteen minutes of ECG recording was completed to measure HRV indices [root mean square deviation of N-N intervals (SDNN), root-mean-square variations of consecutive N-N intervals (rMSSD)] and frequency-domain [low-frequency (LF) power, high-frequency (HF) power and total power (TP)], subsequently, mentioned HRV indices were procured. Pre- and post-PCI measurements were done for each parameter.

**Results:** On admission, PEP and PEP/LVET ratios were higher when compared to 24h post-PCI. LVET increased in 24h post-PCI and sustained at 6 months when compared to the values obtained on admission. Besides, $QS_2$ increased at 24h post-PCI and decreased at 3-month which did not reach baseline even after 6 months of follow-up. In addition, admission SDNN, rMSSD, TP, LF, HF, and HFnu values were higher when compared to 24h post-PCI with the LFnu and LF/HF ratios being lesser. Further, when compared to 24h post-PCI HRV values, there was a rise in SDNN, rMSSD, LF power, HF power, and HFnu with a fall in LFnu and LF/HF ratios at 3- and 6-month post-PCI which did not reach admission values even after 6-months following revascularisation. Further, Major adverse cardiac events (death and re-acute myocardial infarction) occurred in 12 out of 197 IHD patients, during a follow-up of six months. On correlation analysis, measures of STI correlated well with HRV. Further on regression analysis, these modifications in neurocardiac regulation measurements were connected with risk variables and medicines.

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Pivatelli, Flávio, Marcio dos Santos, Gislaine Fernandes, Marcio Gatti, Luiz de Abreu, Vitor E Valenti, Luiz Carlos M Vanderlei, Celso Ferreira, Fernando Adami, Tatiana Dias de Carvalho, Carlos Bandeira de Mello Monteiro, and Moacir Fernandes de Godoy. "Sensitivity, specificity and predictive values of linear and nonlinear indices of heart rate variability in stable angina patients", International Archives of Medicine, 2012.

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EVALUATION OF SYSTOLIC TIME INTERVALS AND HEART RATE VARIABILITY AS INDICATORS OF CARDIAC AUTONOMIC FUNCTION AMONG MALE ISCHEMIC HEART DISEASE PATIENTS ABSTRACT Background and Objectives: Ejection fraction measurements are used to examine the systolic performance of the left ventricle (LV). Due to the ease of measurement, systolic time intervals (STI) are ideally suitable for studying LV performance. Heart rate variability (HRV) is the variation in heart rate from beat to beat and is a crucial method for examining the function of the autonomic nervous system of the heart. Ischemic heart disease (IHD) patients are frequently thought to be in a sympathetically predominant state. Percutaneous coronary intervention (PCI) for the management of myocardial ischemia may help to regain autonomic balance. Hence, this study was planned to gauge STI and HRV measures, after PCI in patients with IHD. Materials and Methods: A total of 229 male IHD patients listed for coronary angiography were enrolled. Among them, 197 male IHD patients (aged 54.09 ± 11.75 years) were included in this study. Out of the included 145 patients went through PCI. In accordance, to calculate the STI [pre-ejection period (PEP), Left ventricular ejection time (LVET), and the total electro- mechanical systole (QS2)] 2D and pulsed-Doppler echocardiogram recording was done. In addition, fifteen minutes of ECG recording was completed to measure HRV indices [root mean square deviation of N-N intervals (SDNN), root-mean-square variations of consecutive N-N intervals (rMSSD)] and frequency-domain [low-frequency (LF) power, high-frequency (HF) power and total power (TP)], subsequently, mentioned HRV indices were procured. Pre- and post-PCI measurements were done for each parameter. Results: On admission, PEP and PEP/LVET ratios were higher when compared to 24h post-PCI. LVET increased in 24h post-PCI and sustained at 6 months when compared to the values obtained on admission. Besides, QS2 increased at 24h post-PCI and decreased at 3-month which did not reach baseline even after 6 months of follow-up. In addition, admission SDNN, rMSSD, TP, LF, HF, and HFnu values were higher when compared to 24h post-PCI with the LFnu and LF/HF ratios being lesser. Further, when compared to 24h post-PCI HRV values, there was a rise in SDNN, rMSSD, LF power, HF power, and HFnu with a fall in LFnu and LF/HF ratios at 3- and 6-month post-PCI which did not reach admission values even after 6-months following revascularisation. Further, Major adverse cardiac events (death and re-acute myocardial infarction) occurred in 12 out of 197 IHD patients, during a follow-up of six months. On correlation analysis, measures of STI correlated well with HRV. Further on regression analysis, these modifications in neurocardiac regulation measurements were connected with risk variables and medicines. Conclusion: Present study could efficiently evaluate STI and HRV. Findings suggest that patients with IHD who underwent PCI infer altered cardiac autonomic balance with this surgical procedure. Yet there was a gradual reversal of sympathetic dominance and restoration of parasympathetic tone on follow-up. The present study still has limitations regarding HRV's subsequent sensitivity and specificity. Particularly, it has a modest specificity (61% to 73%) and a higher sensitivity (43% to 86%). Hence, this method might have impending applications in the management of IHD. Additionally, these measures possibly are potentially used as prognostic tools in future studies. INTRODUCTION Coronary artery disease (CAD) is a major health crisis that affects nearly half the middle-aged people and accounts for approximately to one-third of all deaths. (Prabhakaran D et al. 2016) The leading causes of cardiovascular disease (CVD) mortality in India are ischemic heart disease (IHD) and cerebrovascular accidents, which account for more than 80% of all CVD deaths. Heart failure may not develop as quickly if the right therapy is started early. (Reddy S et al. 2010) The term CAD is also called as coronary heart disease. Ischemic heart disease results because of the reduced blood flow to the cardiac muscle due to atherosclerosis in the coronaries. (Lewis RP et al. 1970, Takase B et al. 1992, Weissler AM et al. 1968) Coronary artery disease comprises of angina pectoris, crescendo angina, heart attack, and sudden cardiac death. (Weissler AM et al. 1977) Systolic Time Intervals (STI) measurement is a well-known non-invasive technique for the quantitative assessment of left ventricular (LV) functioning (Hassan S, Turner P 1983) in health and disease; remains important for clinical use (Lewis RP et al. 1970) and forms no burden to the subjects. (Takase B et al. 1992) Intervals in the cardiac cycle can be defined with the 2 concurrent recording of the heart sounds, the carotid artery pulse tracing, and the electrocardiogram. (Lewis RP et al. 1970, Takase B et al. 1992, Weissler AM et al. 1968, Weissler AM et al. 1977) Sometimes, methodological issues with recording phonocardiograms or indirect carotid pulses preclude the identification of STIs. Currently, most diagnostic facilities offer a non-invasive and safe aortic valve echocardiography procedure. STI is measured using the current approach, which also employs 2D echocardiography and pulsed-Doppler imaging to appraise the left ventricular systolic performance. "Heart rate variability (HRV) is the beat-to-beat difference in heart rate and it occurs as a result of the active influence of the sympathetic and parasympathetic nerve fibers on the Sinoatrial node". (Kuzemczak M et al. 2016, Compostella L et al. 2017) It is a crucial non-invasive instrument for researching the activity of the involuntary nervous system in the heart.11 Higher heart rate variability indicates good compliance with environmental and physiological requirements while lower heart rate variability shows the probable occurrence of cardiovascular threat.11 "Additionally, the vast majority of investigations revealed that the relationship between HRV and mortality was higher when parameters were assessed within the first two weeks following a MI, and few time-domain indices still had predictive significance six months after the end of the study period. A drop in HRV has been found to be a potent and independent predictor of death following ST-segment elevation acute myocardial infarction (STEMI). The predictive significance of HRV indices evaluated 24h after percutaneous coronary intervention (PCI), however, is less well understood. Hence, to assess the sensitivity, specificity, and predictive value of the HRV evaluated 24h post-PCI in predicting the occurrence of major adverse cardiac events (MACE) in patients with acute coronary syndrome (ACS) was the goal of this study in light of the foregoing." (Pernaje Seetharam S et al. 2022) Further, we investigated patients' quality of life using the Short Form-12 (SF-12) health survey questionnaire. (Ware J, Sherbourne CD

17/1/23

Professor & Head of the Department of Physiology Sri Devaraja Urs Medical College Tamaka Kolar

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## TABLE OF CONTENTS

# ABSTRACT

**Background and Objectives:** Evaluation of Left ventricular (LV) systolic function is based on ejection fraction assessment. Due to the ease of measurement, systolic time intervals (STI) are ideally suitable for studying LV performance. Heart rate variability (HRV) is the variation in heart rate from beat-to-beat and is a crucial non-invasive method for examining the function of the autonomic nerve system of the heart. Ischemic heart disease (IHD) patients are frequently thought to be in a sympathetically predominant state. Percutaneous coronary intervention (PCI) for the treatment of myocardial ischemia may help to regain autonomic balance. Hence, this study aimed to evaluate STI and HRV measures, after successful revascularisation by PCI among IHD patients.

**Materials and Methods:** A total of 229 consecutive male IHD patients with acute coronary syndrome planned for coronary angiography were recruited. Among them, 197 patients (aged 54.09 ± 11.75 years) were included in this study. Out of the included 145 patients underwent PCI. In accordance, to calculate the systolic time intervals [pre-ejection period (PEP), and LV ejection time (LVET), and total electro-mechanical systole ($QS_2$)] 2D and pulsed-Doppler echocardiography was performed. In addition, fifteen minutes of ECG recording was done to measure short-term HRV indices and time- [root mean square deviation of N-N intervals (SDNN), root-mean-square of consecutive N-N intervals variations' (rMSSD)] and frequency-domain [low-frequency (LF) power, high-frequency (HF) power and total power (TP)] HRV indices were evaluated. Pre- and post-PCI measurements were taken for each measurement. Further, the Short Form-12 health survey questionnaire has been used to examine patients' quality of life (QoL) post-PCI.

**Results:** On admission, PEP and PEP/LVET ratios were higher when compared to 24h post-PCI. LVET increased in 24h post-PCI and sustained at 6 months when compared to the values obtained on admission. Besides, $QS_2$ increased at 24h post-PCI and decreased at 3-month which did not reach baseline even after 6 months of follow-up. In addition, admission SDNN, rMSSD, TP, LF, HF, and HFnu values were higher when compared to 24h post-PCI with the LFnu and LF/HF being lesser. Further, when compared to 24h post-PCI HRV values, there was an increase in SDNN, rMSSD, LF, HF, and HFnu with a decrease in LFnu and LF/HF at 3- and 6-month post-PCI which did not reach baseline even after 6-months following revascularisation. Further, major adverse cardiac events (death and re-acute MI) occurred in 12 (6.1%) out of 197 IHD patients, during a follow-up of six months. When compared to the SF-12 mental component score, which over time appears to improve without achieving statistical significance, physical component score was found to have significantly improved. We discovered a substantial positive connection between left ventricular ejection fraction and QoL among ACS patients who had not experienced a MACE. Also, on correlation analysis, measures of STI correlated well with HRV. Further on regression analysis, these modifications in neurocardiac regulation measurements were connected with risk variables and medicines.

**Conclusion:** Present study could efficiently evaluate STI and HRV. Findings suggest that patients with IHD who underwent PCI infer altered cardiac autonomic balance with this surgical procedure. Yet there was a gradual reversal of sympathetic dominance and restoration of parasympathetic tone on follow-up. The present study still has limitations regarding HRV's subsequent sensitivity and specificity. Particularly, it has a modest specificity (61% to 73%) and a higher sensitivity (43% to 86%). Hence, this method might have impending applications in the management of IHD. Additionally, these measures possibly are potentially used as prognostic tools in future studies.

# *INTRODUCTION*

# INTRODUCTION

Coronary artery disease (CAD) is a major health crisis that affects nearly half the middle-aged people and accounts for approximately one-third of all deaths. (**Prabhakaran D *et al.* 2016**) Ischemic heart disease (IHD) and stroke are the predominant causes and are responsible for more than 80% of cardiovascular disease (CVD) deaths in India. Initiation of appropriate therapy at early stages may delay the development of heart failure. (**Reddy S *et al.* 2010**)

The term CAD is also called coronary heart disease (CHD) or IHD. Ischemic heart disease includes the reduction of blood flow to the cardiac muscle due to atherosclerosis in the coronary arteries. (**Lewis RP *et al.* 1970, Takase B *et al.* 1992, Weissler AM et al. 1968**) Coronary artery disease comprises stable angina, unstable angina, myocardial infarction, and sudden cardiac death. (**Weissler AM *et al.* 1977)**

Systolic Time Intervals (STI) measurement is a well-known non-invasive technique for the quantitative assessment of left ventricular (LV) functioning (**Hassan S, Turner P 1983**) in health and disease; remains important for clinical use (**Lewis RP *et al.* 1970**) and forms no burden to the subjects. (**Takase B *et al.* 1992)** Intervals in the cardiac cycle can be defined with the concurrent recording of the heart sounds, the carotid artery pulse tracing, and the electrocardiogram. (**Lewis RP *et al.* 1970, Takase B *et al.* 1992, Weissler AM et al. 1968, Weissler AM *et al.* 1977**) Methodological difficulties in recording phonocardiogram or indirect carotid pulse at times prevent determination of the STIs. Aortic valve echocardiogram represents a non-invasive and harmless technique, currently available in most diagnostic centers. The current method uses electrocardiography, 2D-echocardiography, and Pulsed-Doppler imaging, to measure STI and hence, to assess LV systolic function. (**Reant P *et al.* 2010**)

Heart rate variability (HRV) is the beat-to-beat difference in heart rate and it occurs as a result of the active influence of the sympathetic and parasympathetic nerve fibers on the Sinoatrial node. (**Kuzemczak M *et al.* 2016**, **Compostella L *et al.* 2017)** It is a vital non-invasive tool to study cardiac autonomic nervous system activity.[11] Higher HRV indicates good compliance with environmental and physiological requirements while lower HRV shows the probable occurrence of cardiovascular threat.[11]

"Controversies exist regarding HRV measures to assess cardiac autonomic function. Alternatively, pre-ejection period a component of STI may help in assessing cardiac sympathetic activity to accompany the cardiac parasympathetic activity of HRV (HF-HRV)." (**Michael S *et al.* 2017**) In this regard, we hypothesized that monitoring of systolic time intervals and heart rate variability may be a helpful non-invasive, cost-effective approach to explore cardiac autonomic function among ischemic heart disease patients with acute coronary syndrome before and after successful percutaneous coronary intervention.

The autonomic behavior of males and females are different (**Korobka IE *et al.* 2017**) and can be influenced by different phases of the menstrual cycle. Hence in this study, we have planned to recruit only male subjects.

Further, we investigated patients' quality of life using the Short Form-12 (SF-12) health survey questionnaire. (**Ware J, Sherbourne CD 1992, Melville MR *et al.* 2003, Failde I *et al.* 2009)** "The SF-12 questionnaire consists of eight health concepts representing physical functioning; role-limitations due to physical health problems, bodily pain, general health, energy/fatigue, social functioning, role-limitations due to emotional problems, and mental health. The 12 questions in this instrument assess health-related quality of life (HRQoL) in the past four weeks, producing two different 0-100 scores namely physical component (PCS)

and mental component (MCS) scores. The results of the SF-12 with a higher score indicate a better quality of life." (**Ware J, Sherbourne CD 1992**)

"The vast majority of investigations revealed that the relationship between HRV and mortality was higher when parameters were assessed within the first two weeks following an MI, and few time-domain indices still had predictive significance six months after the end of the study period. A drop in HRV has been found to be a potent and independent predictor of death following ST-segment elevation acute myocardial infarction (STEMI). The predictive significance of HRV indices evaluated 24h after percutaneous coronary intervention (PCI), however, is less well understood. Hence, to assess the sensitivity, specificity, and predictive value of the HRV evaluated 24h post-PCI in predicting the occurrence of major adverse cardiac events (MACE) in patients with acute coronary syndrome (ACS) was the goal of this study in light of the foregoing." (**Pernaje Seetharam S *et al.* 2022**)

## CORONARY CIRCULATION

Two major arteries arise from the root of the aorta just above the aortic valve.[13]

a. **Right Coronary Artery**: Provides blood to the right atrium, right ventricle, SA, AV nodes, and sometimes part of posterior LV.[13]

b. **Left Coronary Artery**: Branches into left anterior descending and circumflex arteries. Supplies LA, LV, septum.[13]

In 50% of individuals, the right coronary artery has a greater flow (right dominance); the left coronary has a greater flow in 20% (left dominance), and the flow is equal in 30% (Co-dominance). The coronary sinus and anterior cardiac veins, which drain into the right atrium, return the majority of venous blood to the heart. In addition, the arteriosinusoidal vessels, thebesian veins; and a few arterioluminal vessels drain directly into the cardiac chambers.[13]

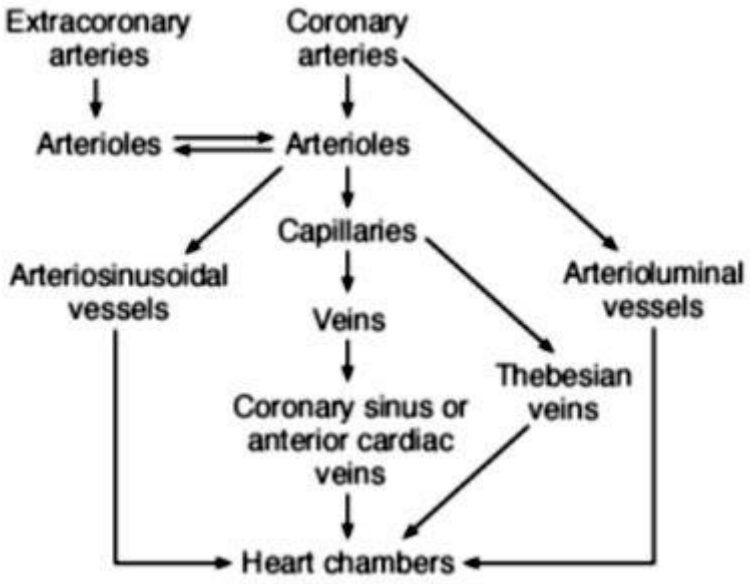



***Fig 1. Coronary artery circulation.***[26]

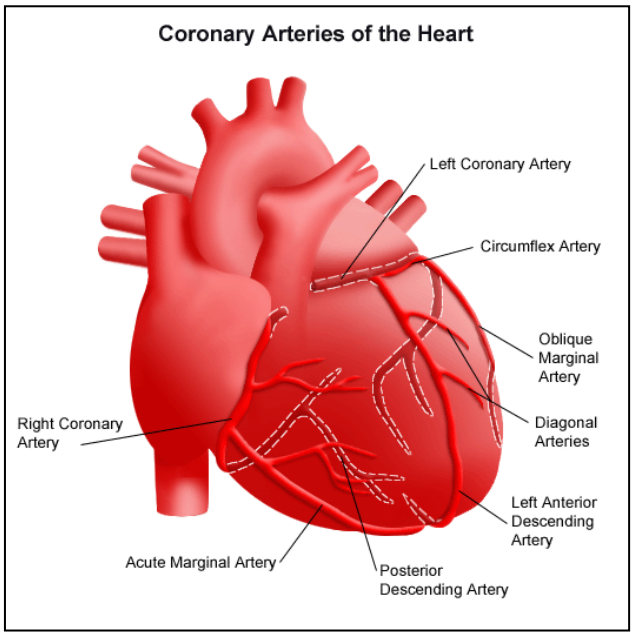



***Fig 2a.***

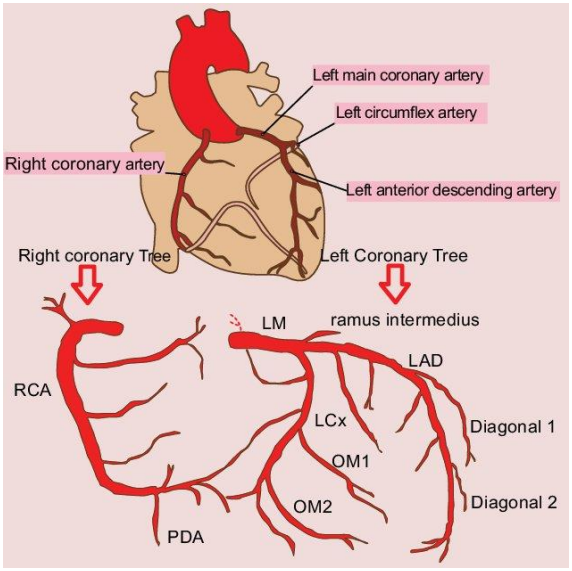



***Fig. 2b***

***Fig 2 a-b. Coronary arteries and their principal branches.[26] OM: obtuse marginal; PDA: posterior descending artery; RCA: right coronary artery.***

## CARDIAC CYCLE

The **cardiac cycle** refers to the sequence of events that occur from the start of one heartbeat to the start of the next. The cardiac cycle consists of **diastole**, a time of rest during which the heart fills with blood, followed by **systole**, a period of contraction.[30]

**Ejection fraction**[30] is the percentage of the end-diastolic volume that is ejected, which is normally around 60%.

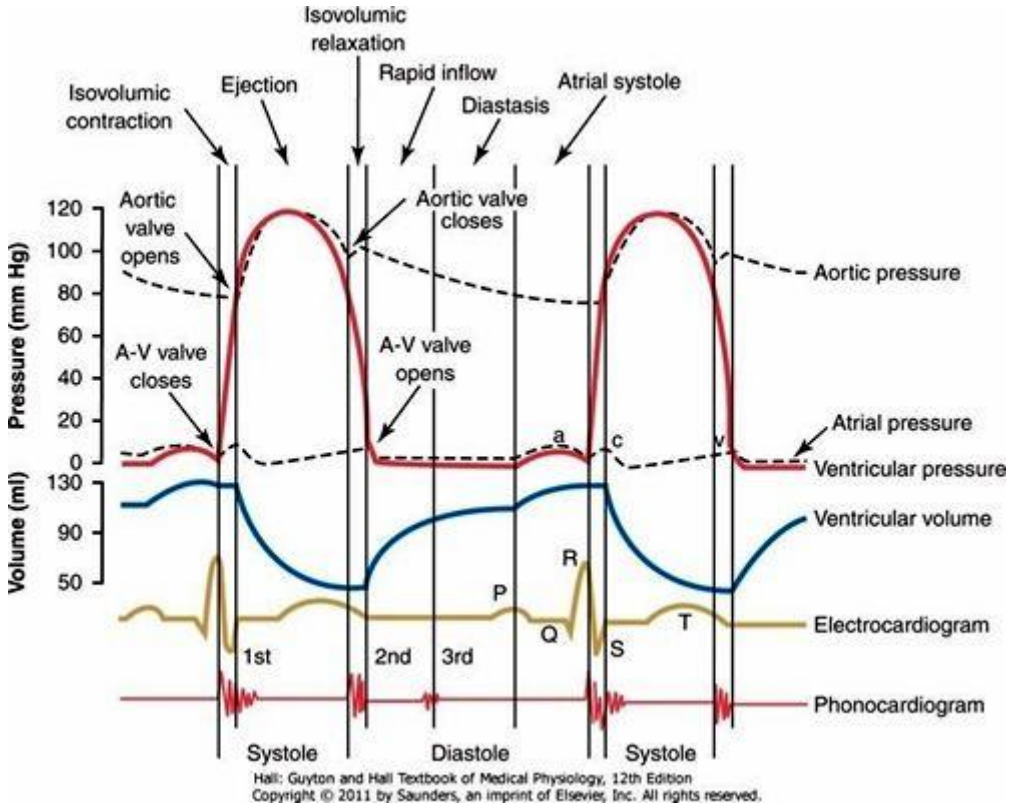



***Fig 3. Cardiac Cycle[30]***

**AUTONOMIC NERVOUS SYSTEM**

The cardiovascular system is under the control of the autonomic nervous system (ANS). Short-term control of heart rate and blood pressure in everyday situations is done by the ANS. Heart rate is under the control of two branches of the autonomic nervous system: the parasympathetic and sympathetic nervous systems. Parasympathetic (vagal) modulation releases the hormone acetylcholine to decrease the heart rate and cardiac contractility, whereas, the activity of the sympathetic branch releases the hormone - epinephrine and norepinephrine to accelerate the heart rate and regulates peripheral vasoconstriction.[30]

Balanced cardiac ANS function is based on strong parasympathetic and efficient sympathetic modulation of the heart. Effective ANS modulation has been linked with reduced risk of cardiovascular complications.[36]

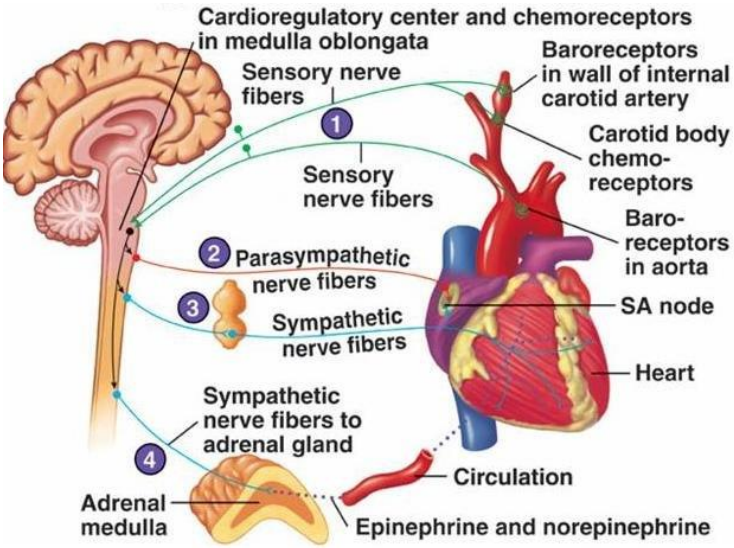



*Fig 4. Nerve supply to the heart/Cardiac autonomic innervation.*[36]

## PATHOPHYSIOLOGY OF MYOCARDIAL INFARCTION

A heart attack results when an artery to the heart muscle becomes completely blocked and the heart muscles fed by that artery die. When the blood supply to a portion of the myocardium is cut off, the myocardium undergoes dramatic changes that result in irreversible changes and the death of muscle cells.[4]

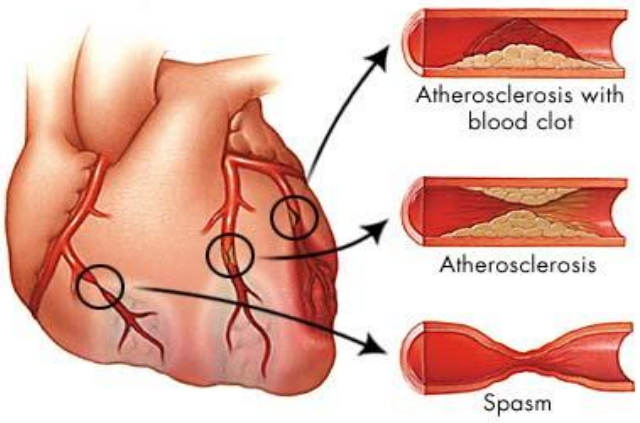



***Fig 5. Coronary artery disease***

***Signs and symptoms***

**Symptoms:** Chest pain (angina), weakness, lightheadedness/fainting, nausea, a cold clammy skin, pain or discomfort in the arms or shoulders, and dyspnea.[4]

***Risk factors associated with ischemic heart disease***

Physical inactivity, (**Lee IM *et al.* 2012**) history of (H/O) cigarette smoking or current smoker: 1/5/10 cigarettes/day.[29,58] H/O alcohol consumption or current alcoholic: >5 units (One unit equals 10 ml or 8 g of pure alcohol, which is around the amount of alcohol the average adult can process in an hour) of alcohol daily sustained for 3 months duration.[54]

***Modifiable risk Factors associated with IHD***

Elevated blood pressure of 140/90 mmHg or higher, Hypercholesterolemia and elevated triglycerides with high LDL cholesterol over 100 mg/dL and low HDL cholesterol under 40 mg/dL, Hyperglycemia with HbA1c >7.0, Being overweight (BMI: 25–29 kg/$m^2$) or being obese (BMI >30 kg/$m^2$), Uncontrolled stress or anger, and Unhealthy Diet.[4]

***Non-modifiable risk factors associated with IHD***

Coronary artery disease[1] is more likely to occur especially after 65 years of age. Men have a greater risk of heart attack than women and men have heart attacks earlier in life than women. However, beginning at age 70, the risk is equal for men and women with the family H/O CHD or other atherosclerotic vascular diseases at an early age (Men <55 years). Further risk of developing heart disease is higher if one has a parent with H/O heart disease, especially if they were diagnosed before age of 50.[4]

## *DIAGNOSIS*

Myocardial infarction[1] is defined by elevated cardiac biomarkers (Troponin I or CK-MB) with a rising or falling tendency and at least one of the following:

Ischemic symptoms, electrocardiogram changes such as ST-segment changes, new bundle branch block or pathologic Q waves, and changes in heart wall motion (presence of regional wall motion abnormality) on imaging.[1]

### *Types*

An acute coronary syndrome is usually diagnosed in the emergency room, when ECGs may be conducted in order to identify "evolving alterations" (indicating continued damage to the cardiac muscle). The ECG is extremely helpful in diagnosing and finding infarctions.[30] If ECG shows elevation of the "ST segment", which in the setting of intense typical angina is strongly suggestive of acute myocardial infarction and is referred to as a **STEMI** (ST-elevation MI). This is treated as an emergency with both immediate coronary angiography and percutaneous coronary intervention (angioplasty with or without stent placement) or thrombolysis, depending on what is available. In case of a lack of ST-segment elevation, heart damage is identified by the presence of cardiac markers. Then the chest discomfort is attributed to a "non-ST elevation MI" (**NSTEMI**) if there is a sign of damage (infarction). When there is no sign of damage, the term "**Unstable angina**" is used. This process usually warrants hospital admission and close monitoring in a coronary care unit for probable complications, such as cardiac arrhythmias.[1]

### *Cardiac biomarkers and their importance*

Different biomarkers are used to define the presence of cardiac muscle damage. **Troponins**, measured through blood tests, are thought to be the best because they are more sensitive and specific than other tests at detecting damage to the heart muscle.[1]

Other tests, such as **CK-MB** or myoglobin, are not advised. For acute myocardial injury, CK-MB is not as specific as troponins, and they could be elevated with previous cardiac surgery, inflammation, or electrical cardioversion; it increases within 4 to 8 hours and comes back to normal within 2 to 3 days.[1]

***Troponin-I***

Troponin-I is a class of cardiac and skeletal muscle proteins. It is a useful marker in the laboratory diagnosis of a heart attack. The paralog which is expressed in human cardiac muscle is Cardiac troponin I (cTnI), TNNI3. The reference range of troponin in healthy persons is very low or undetectable. When troponin levels exceed the reference range, it indicates that your cardiac muscle cells are injured and are leaking troponin into the bloodstream. According to the American Board of Internal Medicine, the reference ranges for the troponin test are expressed in nanograms per milliliter (ng/mL). Hence the reference range of Troponin I is 0 - 0.04 ng/mL. Within three to twelve hours following a heart attack, troponin levels often significantly rise and peak around 24 hours later. They will continue to rise for several days as well.[5]

***CK-MB or myoglobin***

The CK-MB test also referred to as the CPK-MB test (creatine phosphokinase-MB), is a cardiac marker used to help detect acute myocardial infarction, myocardial ischemia, or myocarditis.[2]

***Electrocardiography***

Electrocardiography is the graphical recording of the heart's electrical activity. The three main components of an ECG are: The P wave, which represents atrial depolarization; the QRS complex, which represents ventricular depolarization; and the T wave, which denotes repolarization of the ventricles. Ischemia or NSTEMIs could manifest as ST-segment

depression or T wave inversions. The earliest sign of STEMIs is hyperacute T waves, peaked T waves owing to local hyperkalemia in myocardial ischemia. This then progresses over a period of minutes indicated by the elevations of the ST-segment by at least 1 mm. Over a period of hours, a pathologic Q wave possibly will appear and the inversion of T wave will be there. Over a period of days, the resolution of ST-elevation will happen. Pathologic Q waves usually remain forever. The location of ST-elevation in a STEMI can be used to pinpoint the coronary artery that has been blocked. The anterior wall of the heart is supplied by the left anterior descending artery, and therefore roots ST-elevations in anterior leads (V1 and V2). The left circumflex artery supplies the lateral part of the heart and hence causes ST-elevations in lateral leads (I, aVL, and V6). The inferior aspect of the heart is supplied by the right coronary artery, and consequently causes ST-elevations in inferior leads (II, III, and aVF).[3]

***Transthoracic Echocardiography***

The transthoracic echocardiogram uses ultrasound to create a still or moving image of the heart's interior structures. In this instance, several images of the heart are obtained by placing the probe (or ultrasonic transducer) on the subject's chest. It serves as a non-invasive way to evaluate a patient's heart's overall health, including the condition of their heart valves and the strength of their heart muscle contraction (an indicator of the ejection fraction). The pictures are recorded after being shown in real-time on a monitor.[6]

**Blood flow can be improved by** placing a stent within the vessel to expand the lumen, using intracoronary balloon angioplasty to stretch the vessel open, and bypassing the diseased vessel with a vascular graft (coronary artery bypass grafting).

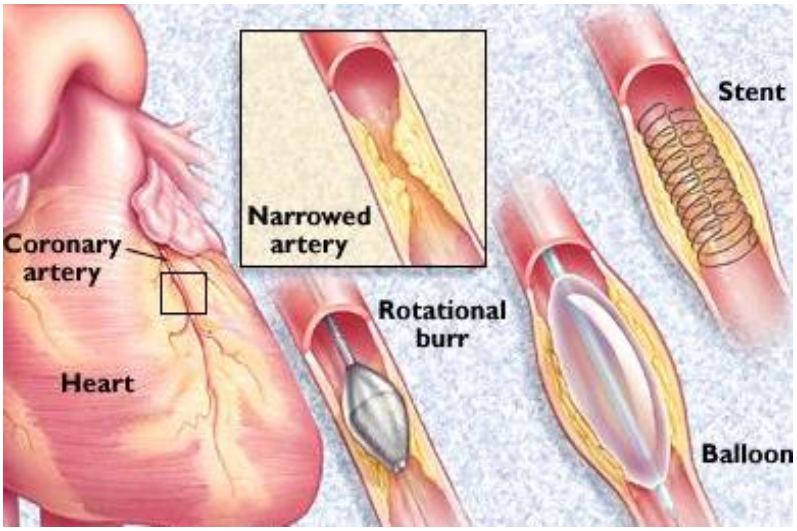



***Fig 6. Rotational burr, Balloon angioplasty and stent placement***

# *NEED FOR THE STUDY*

# NEED FOR THE STUDY

1. Monitoring of systolic time intervals (STI) and heart rate variability (HRV)[46, 63] may be a valuable, non-invasive, and cost-effective approach to investigating cardiac autonomic function among ischemic heart disease (IHD) patients with acute coronary syndrome.

2. Correlation between STI and HRV to evaluate cardiac autonomic function among IHD patients' needed attention.

3. Initiation of appropriate therapy at the early stages of IHD may delay the development of heart failure. (**Reddy S *et al.* 2010**)

4. There was a need to understand the effects of IHD on health-related quality of life (**Bahall M, Khan K 2018**) among post-PCI patients.

# *REVIEW OF LITERATURE*

# REVIEW OF LITERATURE

**Prabhakaran D *et al.* 2016** reported that cardiovascular illness has now become the leading cause of death in India. The Global Burden of Disease study guess of the age-standardized cardiovascular disease death rate of 272 per 100,000 people in India is more than the global average of 235 per 100,000 people. Some aspects of the cardiovascular defect outbreak in India are notable elements of concern, including its accelerated upsurge, the early age of disease inception in the population, and the elevated case fatality rate.

**Reant P *et al.* 2010** studied the usefulness of STI measurement by the pulsed-Doppler echocardiography among 134 heart failure (HF) patients and 43 control subjects to evaluate LV systolic function based on ejection fraction assessment. Furthermore, with increasingly changed LVEF, PEP was significantly prolonged, whereas LVET significantly decreased, resulting in a significantly prolonged PEP/LVET. In patients with HF, a correlation between PEP/LVET and LVEF was found (r = 0.55). Based on ROC curve analyses, the area under the curve was found to be 0.91 for PEP/LVET >0.43, which allowed authors to detect LVEF <35% with a sensitivity of 87% and a specificity of 84%. In addition, the authors observed that this method has a potential role in the management of HF patients.

**Failde *et al.* 2009** studied health-related QoL (HRQL) in 186 patients with ischemic cardiopathy, using the SF-36 and SF-12. The mean scores observed were alike in the two questionnaires. High levels of agreement were found, and the corresponding regression model explained 93 and 87 percent of the variability in the PCS-36 and MCS-36, respectively. The SF-12 was equally competent in identifying the differences between

AMI and angina when compared to SF-36. Therefore, the use of SF-12 provides the same facts to be obtained as from the SF-36, with less exertion for the patient and the doctor.

**Michael *et al.* 2017** reported cardiac parasympathetic activity could be investigated using HRV and cardiac sympathetic activity might be investigated using STI. Hence, simultaneous monitoring of HRV and STI could be a valuable non-invasive approach to investigate autonomic stress reactivity with regard to exercise stressors.

**Wiley CR *et al.* 2021** analyzed data from 158 healthy participants (aged 19.09±1.84 years). Cardiac autonomic balance (CAB) and Cardiac autonomic regulation (CAR) values were calculated using both HF and the rMSSD of HRV, along with PEP and LVET of STI. Analysis showed that correlations were significantly weaker between CAB and CAR calculated using LVET for both HF ($p$ <0.001) and rMSSD ($p$ <0.001) than with PEP. Authors suggested that future research should consider calculating CAB and CAR using chronotropic measures for both parasympathetic (HF-HRV) and sympathetic activity (LVET of STI), which could provide more precise and independent measures of cardiac autonomic activity compared to a mixture of inotropic (i.e., PEP) and chronotropic (i.e., HF-HRV) measures.

A cross-sectional study by **Bahall *et al.* 2018** included 534 patients with the first AMI. Enrolled patients belonged to 2 to 10 weeks, 5 to 22 months, and more than 22 months to 4 years post-AMI periods. Quality of Life (QOL) of patient's post-AMI was evaluated using the Quality of Life after Myocardial Infarction questionnaire. Overall QOL was better over time in the Emotional, Physical, and Social domains. Lower QOL was observed in patients with IHD in the Physical domain only; among women, in NSTEMI patients, and diabetes patients in all domains; in patients with hypertension and renal disease only in the Physical and Social domains. Alcohol consumption was associated

with better QOL while self-reported stress and lack of exercise were related to lower QOL. With aging, QOL in the Physical domain was found to be declined. Hypercholesterolemia and smoking showed no association with QOL.

**Pivatelli *et al.* 2012** found that parasympathetic activity was decreased in CAD patients, and various HRV indices, including HF in relative units, rMSSD, and the number of adjacent N-N intervals that differed by greater than 50 milliseconds, might be used to predict prognosis in chronic stable angina patients.

**Sharma R *et al.* 2012** measured the STI namely $QS_2$, LVET, PEP, and LVET/PEP by the simultaneous recording of an electrocardiogram, carotid artery pulse and phonocardiogram among 58 young healthy male volunteers (aged 18-45 years). In addition, authors assessed their sympathetic functions by hand grip dynamometer test and cold pressor test while parasympathetic functions were assessed with the help of a 30:15 ratio and Valsalva ratios. STI's were corrected for heart rate to find out the correlation between STIs and autonomic functions. No significant correlation between different STIs and autonomic functions was observed.

**Coviello I *et al.* 2013** assessed the prognostic value of HRV in STEMI patients treated by PTCA and optimal medical therapy. One hundred and eighty-two consecutive patients with a first STEMI (59.1±8.11 years; 82.4% men) treated by primary PTCA were considered. HRV was assessed by 24-hour Holter ECG recordings before discharge, 1, and 6 months after discharge. The primary endpoint was the occurrence of Major adverse cardiac events (MACE), defined as death or re-AMI. At a follow-up of 42±23 months, MACE occurred in 14 patients (7.6%; 3 deaths and 11 re-AMIs). HRV parameters before discharge were significantly lower in patients with MACE, with SDNN, very LF, and LF amplitude being the most predictive variables.

**Abrootan S *et al.* 2015** included 64 patients with chronic stable angina, consisting of 27 males and 37 women, with an average age of 56.8±9.1 years. Only the difference between pre- and post-revascularization SDNN was found to be statistically significant ($p$ = 0.013).

**Venkatesh D *et al.* 2018** concluded that sympathetic predominance with lowered parasympathetic activity observed in CAD patients puts them at a higher risk of adverse cardiac events. An attempt needs to be made to incorporate improvement of HRV as a modality of treatment of CAD.

A prospective observational study by **Sorensen *et al.* 2018** included African-Americans (n=1980) of the Atherosclerosis Risk in Communities (ARIC). Subjects underwent echocardiography and LVET was measured using pulsed-wave Doppler. A short LVET was associated with younger age, in case of men, an increase in diastolic blood pressure, and the prevalence of diabetes, tachycardia, and elevated blood sugar levels. During a median follow-up of 17.6 years, 384 of them had an incidence of HF, 158 had a myocardial infarction, and 587 of them died. In univariate analysis, a lower LVET was significantly associated with increased risk of all events ($p$ <0.05 for all). Nevertheless, after multivariable adjustment for confounding variables, LVET persisted as an independent interpreter only of incident HF [hazard ratio 1.07, $p$ = 0.010 per 10 ms decrease]. In addition, LVET provided incremental prognostic information on the risk of future HF and death but not myocardial infarction.

Another study by **Wennerblom *et al*. 2000** included 48 patients with angina and 41 age-matched healthy controls, 24h Holter recordings were done before the coronary intervention, 1- and 6-months post-revascularization. The authors observed normal SDNN, SDANN, and LF/HF ratio with a significant reduction in rMSSD, pNN50, total

power, LF, and HF peak among angina patients compared to controls. Hence, it was shown that successful revascularization would cause only a partial stabilization of vagal tone indicating that ischemia could be one of the mechanisms of the reduction in HRV among chronic CAD patients.

**Gomes *et al*. 2009** found that in patients with myocardial ischemia, cardiac revascularization decreased central sympathetic activation. In their investigation, a two-channel Holter was utilized to record for ten minutes and determine the mean LF/HF ratio. The ratio was shown to decrease following revascularization.

**Miyase *et al.* 2014** disclosed that prior to coronary angiography, calculating the LF/HF ratio can be used to determine whether CAD is present. It has been discovered that in the case of CAD, a considerable decline in HRV parameters is a predictor of death.

**Forslund *et al*. 2002** discovered that frequency domain HRV indices, obtained from 24-hour Holter monitoring, showed significant predictive value for the risk of cardiovascular mortality in patients with chronic stable angina. Additionally, it was demonstrated that, regardless of other co-morbidities, a low HRV was an effective clinical risk indicator in individuals with sinus rhythm and the greatest predictor of angiographic coronary disease.

A review by **Benichou *et al.* 2018** included 25 case-control studies; which consisted of 1,356 patients with T2DM and 1,576 healthy controls. T2DM patients had significantly reduced R-R intervals, SDNN, rMSSD, pNN50, TP, LF, and HF. An overall decrease in the HRV of T2DM patients could be explained by the detrimental effects of varied glucose metabolism on HRV, leading to cardiac autonomic neuropathy.

In a study by **Harris *et al.* 2014** 24-hour Holter recordings of 279 patients with ACS were done within 45 minutes of arrival at an emergency department. During the 1-year follow-

up, 82 were re-hospitalized, 17 died, and 94 patients survived. Predictors of re-admission included high HFnu, reduced LFnu, and low LF/HF ratio. Natural logs of TP and ultra-low frequency power variables were significantly associated with the death.

**Makikallio *et al.* 2001** measured the standard deviation of R-R intervals, HRV index, and frequency-domain indexes from 24-hour Holter recordings in 499 patients with congestive heart failure and LVEF ≤ 35%. During a mean follow-up of 665±374 days, 210 (42%) deaths occurred. Conventional HRV indexes predicted mortality by univariate analysis. In NYHA functional class II, all HRV indexes were more significant univariate predictors of mortality than in class III or IV. Furthermore, among patients with moderate heart failure, HRV measures provided prognostic information, when compared to patients with utmost severe functional impairment.

A study conducted in India by **Huffman *et al.* 2019** collected health-related QOL data from 1261 participants (aged 60.8±13.7 years, 62% men) in the Acute Coronary Syndrome Quality Improvement in Kerala trial. The study used Seattle Angina Questionnaire administered 30 days post-discharge for AMI. The frequency of angina was higher, physical limitations, lower treatment satisfaction, and QOL was seen among older patients.

**González-Chica *et al.* 2017** examined the impact of preventive healthcare on the HRQoL of 2379 South Australian adults who were either obese, had metabolic risk factors, had cardiovascular disease, or were healthy. Assessment of Physical (PCS) and mental components scores (MCS) of HRQoL were done using the SF-12 questionnaire. Individuals with CVD were unlikely to have adequate alcohol consumption (63.4%; $p$ = 0.026), but those achieving the recommendation had lesser PCS. Non-smoking was alike in all groups (85%; $p$ = 0.768) and was associated with a superior MCS only among

healthy individuals and CVD patients. In all the groups, participants attaining all the lifestyle recommendations had an improved PCS. Only 48.2% of patients with CVD reported collective use of antithrombotic, antihypertensive, and antilipidemic drugs, nevertheless, the use of these drugs was not related to HRQoL.

**Anchah *et al.* 2017** enrolled 112 patients with newly identified ACS. Authors compared the pre- and post-quality of life of three groups [intervention (modified Cardiac Rehabilitation Programme/MCRP), conventional, and control] at baseline, 6 months, and 12 months post-discharge. Short-Form 36 Questionnaire was used to procure QoL data. In all three groups at baseline, the physical and mental health summaries showed poorer results. After the 6-month follow-up, the physical component summary (PCS) defined in the Modified CRP subjects was better, but lower in the mental component summary. At the end of the 12-month follow-up, the MCRP participants accomplished well in their PCS than those in the conventional CRP and control groups.

In another study on cardiac rehabilitation by **Azmi *et al.* 2015** data was collected from ACS patients. At baseline and at 12 months QoL data were acquired using a validated version of the EuroQol five-dimensional questionnaire. Visual analogue scale scores and utility rates from Malaysia and the UK were used to calculate health utility scores. The preceding study's data from 104 participants were utilized. At baseline, the mean utility score was 0.75, and at 12 months, it was 0.82. According to the Malaysian tariff, there was a statistically significant improvement in utility from the baseline to 12 months, but not according to the UK tariff.

**Chen *et al.* 2018** enrolled three groups of heart failure patients with: preserved LVEF (>50%), mid-range LVEF (40–49%), and reduced LVEF (<40%). The Minnesota Heart Failure Living Questionnaire (MLHFQ) was used to quantify the HRQoL scores. There

were significant differences in the total MLHFQ scores and its subscale scores among the three groups. MLHFQ domains confirmed high internal reliability among the three groups. A significant association between NYHA class in HFrEF and HFmrEF MLHFQ physical subscale scores were observed. Compared with the HFpEF group, in the groups with low MLHFQ scores, the HFmrEF group showed significantly increased rates of death and HF-related hospitalization. Furthermore, the features and clinical outcomes were different among HF patients with different LVEF values.

# *AIMS AND OBJECTIVES*

# AIMS AND OBJECTIVES

**Primary objectives**

1. To estimate systolic time intervals (STI) and heart rate variability (HRV) among ischemic heart disease (IHD) patients before percutaneous coronary intervention (PCI), 24 hours post-PCI, 3- and 6 months post-PCI.
2. To evaluate STI and HRV among IHD patients with and without major adverse cardiac events (MACE).
3. To correlate STI with measures of HRV among IHD patients.

**Secondary Objectives**

4. To estimate the association of risk factors with HRV and STI among IHD patients.
5. To determine the association of quality of life in post-PCI IHD patients with STI and HRV.
6. To study the ability of 24h post-PCI STI and HRV values in predicting the occurrence of MACE among IHD patients.

# *MATERIALS AND METHODS*

# MATERIALS AND METHODS

**4.1 Type of Study:** Prospective cohort study.

**4.2 Study Setting:** R.L. Jalappa Hospital, Tamaka, Kolar.

**4.3 SAMPLE SIZE ESTIMATION**

**4.4 SAMPLE SIZE ESTIMATION**

The sample size for the present study was calculated (**Abrootan S *et al.* 2010**) using nMaster 2.0 software. Considering the time-domain HRV parameter, SDNN (in milliseconds), the standard deviation in the pre-PCI group (Chronic stable angina patients) = ±19.7 ms, and the standard deviation in the post-PCI group = ±41.4 ms.

Minimum expected difference: 41-27.5 = 13.5. Effect size (Cohen's d) = $\mu_2$-$\mu_1$/$SD_{pooled}$ (where SD=standard deviation). Therefore, d = 13.5/30.55 = 0.44. $SD_{pooled}$ = $\sqrt{S1^2+S2^2/2}$. So, $SD_{pooled}$ = 1050.959.

Confidence interval = 99%. Level of Significance/Alpha error = 1%. Statistical Power = 90%. Type of test = two-tailed. Required sample size = 172.

$$n = \frac{2\sigma^2(Z_\beta + Z_{\alpha/2})^2}{\text{difference}^2}$$

Where $\sigma^2$ represents the $SD_{pooled}$; $Z_\beta$ is the statistical power of 90% (1.282); Zα/2 is the alpha error of 1% or 0.010 (2.576); the difference is the effect size or the difference in means.

$$n = 2\ \frac{(1050.959)\ (1.28+2.576)^2}{(13.5)^2}$$

Hence, n = 171.61

Expecting a dropout rate of 10%, the final sample size was planned to be 172+17.2=189.2, which was rounded off to 190.

## 4.5 INCLUSION AND EXCLUSION CRITERIA

***Inclusion criteria***

1. Ischemic heart disease[34] patients with acute/evolved STEMI, NSTEMI, and Unstable angina[17].
2. Gender: male

***Exclusion criteria***

1. Patients with a history of MI or IHD (including bypass surgery and stroke).
2. Patients with psychiatric comorbidities.
3. Patients on anticholinergics, on medications for thyroid disorders.
4. Patients with atrial fibrillation
5. Patients with Parkinson's disease, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, psoriasis, amyloidosis, and malignancies who may have dysautonomias.
6. Hemodialysis patients.

## 4.6 METHODOLOGY

***Ethical clearance***

Obtained from the central ethics committee for the start of the study (SDUAHER/KLR/R & I/91/2021-22 dated 9-3-202).

***Written informed consent***

Details of the study were discussed with all the study participants, and explained to their relatives in their own language of understanding. Recruited participants were informed that at

any point of the study, they have the full right to withdraw or discontinue participating. Before commencing the intended procedure, verbal and written informed consents were obtained.

A thorough history (Personal/Occupational/Diet/Habits), Clinical examination (Past-medical/surgical/family/relevant investigations/medications), General examinations [Vital signs and anthropometric measurements (height and weight); Pain location and scoring; Pallor, clubbing, icterus, edema, emaciated; Body Habitus-Obese/Average built/Thin], Psychological (Anxious/Depressed/Angry/Suicidal/Homicidal), and systemic examinations were carried out for all the study subjects.

Identification of smokers/tobacco usage was done based on the history, nicotine smell, stains on the inner aspect of their teeth and hard palate, nail discoloration, and other signs as appropriate for the identification of smoking. Alcoholics were assessed based on their history or current alcoholic consumption of >5 units of alcohol daily, sustained for 3 months duration.

***Anthropometric measurements***

**Height and Weight:** The height in centimeters (using Bio Plas Inc. Stadiometer, USA) and weight in kilograms (using KRUPS weighing scale, New Delhi, India) of the subjects were measured with shoes removed and minimal clothing on.

Calculation of BMI was based on weight (W) in kilograms divided by height (H) in meters square ($m^2$) formula [$W/H^2$].

***Arterial blood pressure measurement***

At the coronary care unit (CCU), blood pressure was measured manually or the subject was connected to a cardiac monitor with the patient in the supine position. At OPD, systolic and diastolic blood pressures were measured using a sphygmomanometer (model BPDL 237, Dial

BP: clock model by Industrial Electronic & Allied products) with the subjects seated in a chair comfortably.

***Electrocardiography***

At CCU, twelve-lead ECG recording was done using GE Medical Systems Information Technologies (MAC 1200 ST electrocardiograph machine) to assess the changes in the ST-segment to confirm a myocardial infarction.

***A provisional diagnosis of Acute/Evolved STEMI/NSTEMI and unstable angina***

We prospectively studied consecutive patients admitted to our CCU with an acute myocardial infarction, who underwent PCI (primary/elective) of the culprit coronary artery within 6 to 24h of symptom onset in the case of acute STEMI patients, with 70% within 6h of symptom onset. Non-STEMI patients underwent elective PCI within 24h of symptom onset. Patients were also included if they underwent earlier failed thrombolysis (rescue PCI), as indicated by the persistent ST-segment elevation. Symptom-to-door timing in case of evolved MI (STEMI/NSTEMI) and unstable angina patients was 2h to month duration.

Acute STEMI was diagnosed in patients presenting with typical chest pain lasting ≥30 min and associated with ST-segment elevation ≥0.1 mV in ≥2 contiguous leads on the admission ECG. Non-STEMI was diagnosed in patients presenting with typical chest pain lasting ≥30 min and associated with ST-segment depression ≥0.1 mV in ≥2 contiguous leads on the admission ECG, T wave inversion, with the troponin-I positive. Evolved MI was diagnosed with the symptom onset from a few hours to 1 week; from hyperacute T waves to ST-elevation, then T wave inversion in ≥2 contiguous leads on the admission ECG. Unstable angina was diagnosed with the on and off symptom onset from a few hours to 1 month.

The clinical and laboratory parameters recorded for each patient were as follows: cardiovascular risk factors, site of infarction determined by ECG and 2D-echocardiogram, symptom-to-door timing, culprit coronary artery vessels/number of diseased coronaries (defined as the presence of diameter stenosis >50% of coronary arteries as evidenced by CAG), thrombolytic therapy before PCI, thrombolysis in myocardial infarction (TIMI) coronary flow grade post-PCI, peak values of markers of myocardial necrosis [CK-MB or troponin I], and drug therapy.

**Systolic time intervals measurement**

All subjects underwent 2D-echocardiographic evaluation using a Vivid S5 Echocardiograph machine (GE Healthcare systems, Israel, 2008) with a 2.0 to 3.6 MHz transducer. Doppler gains were attuned at a 100 mm/s sweep speed. The standard echocardiogram included an assessment of the left ventricular parasternal long axis (PLAX) view, parasternal short axis (PSAX) view, and apical views (four-, two-, three-chamber views).

"**Systolic time intervals** determined from the 2D-aortic valve echocardiogram based on pulsed-Doppler aortic acquisitions were: **The total electro-mechanical systole ($QS_2$)** is the interval from the onset of Q wave of QRS complex on the ECG to the closure of the aortic valve on the echocardiogram. **Pre-Ejection Period (PEP)** is the interval from the onset of ventricular contraction to the beginning of aortic ejection. **Left Ventricular Ejection Time (LVET)** is the interval ranging from the beginning to the termination of aortic flow." (**Reant P *et al.* 2010**)

***Fig 7a.*** *2D-echocardiography.*

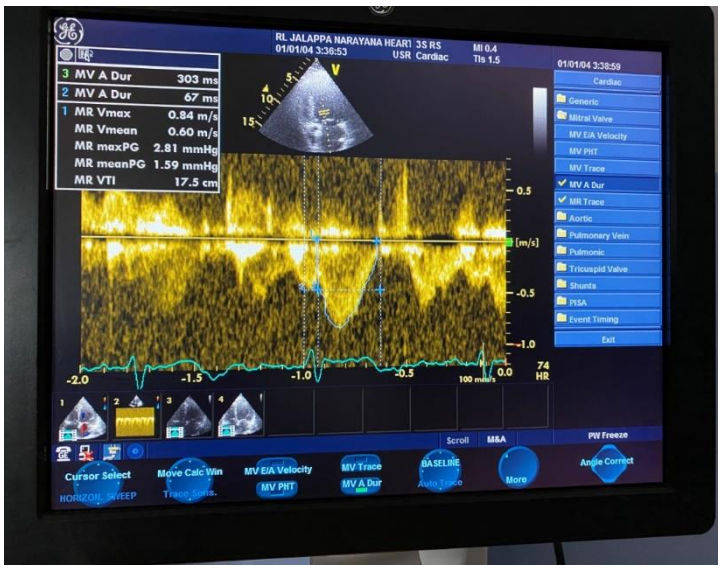



***Fig 7b.*** *Measurements of PEP and LVET in an IHD patient: PEP (2 MV A Dur) = 67 ms, LVET (3 MV A Dur) = 303 ms, PEP/LVET = 0.22.*

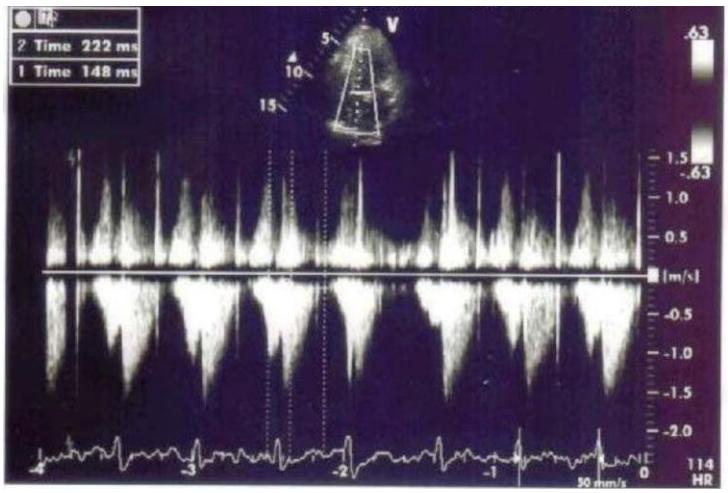



***Fig 7c.*** *Measurements of PEP and LVET in an ischemic heart disease patient on admission for percutaneous coronary intervention: PEP (1 MV A Dur) = 148 ms, left ventricular ejection time (2 MV A Dur) = 222 ms, PEP/LVET = 0.67.*

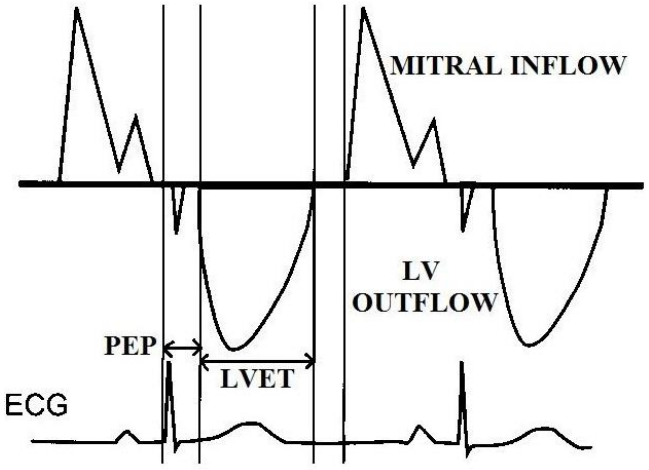



***Fig 7d.*** *Line diagram depicting the measurements of PEP and LVET using pulsed-Doppler echocardiography. ECG: Electrocardiogram; PEP: Pre-ejection period; LVET: Left ventricular ejection time.*

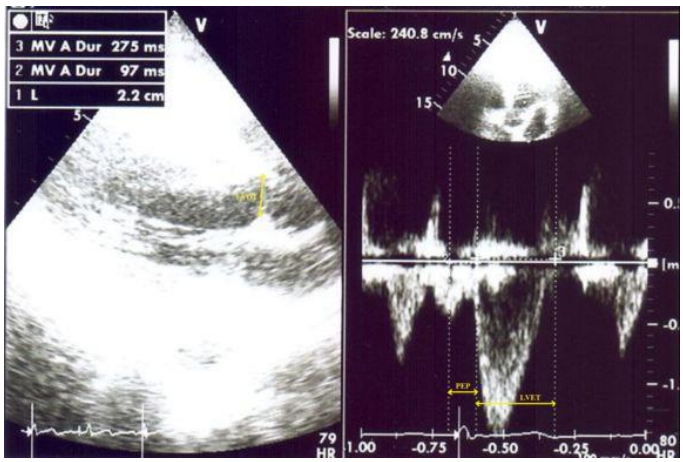



***Fig 7f.*** *Measurements of PEP and LVET in an ischemic heart disease patient 1-week post revascularization with percutaneous coronary intervention: PEP (2 MV A Dur) = 97 ms, left ventricular ejection time (3 MV A Dur) = 275 ms, PEP/LVET = 0.35. The cross-sectional area of the aortic orifice (LVOT: Left ventricular outflow tract or 1 L) = 2.2 cm.*

An echocardiogram assessment will ensure the presence/absence of regional wall motion abnormality. Left ventricular ejection fraction assessment was done according to biplane Simpson's method (**Fig. 8**).

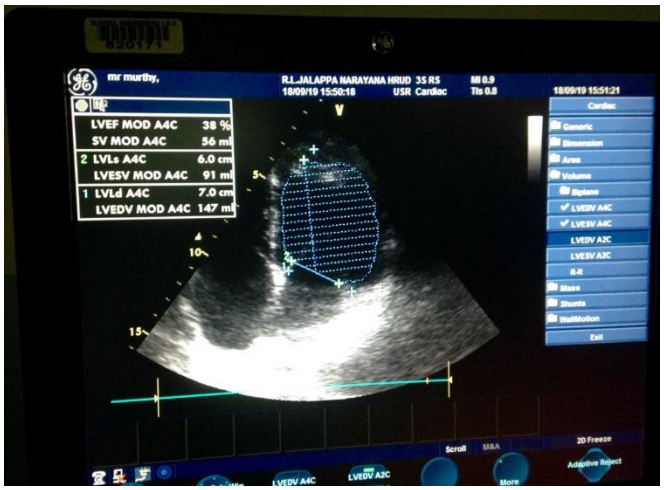



***Fig 8.*** *Left ventricular ejection fraction assessment according to biplane Simpson's method*

Stroke volume was measured using the formula: Cross-sectional area of Aortic Valve (using PLAX view) X Velocity time integral of Mitral regurgitation (with A5C, transducer probe kept 2 mm away from left ventricular outflow tract using pulsed-Doppler echocardiography) (**Fig. 9**).

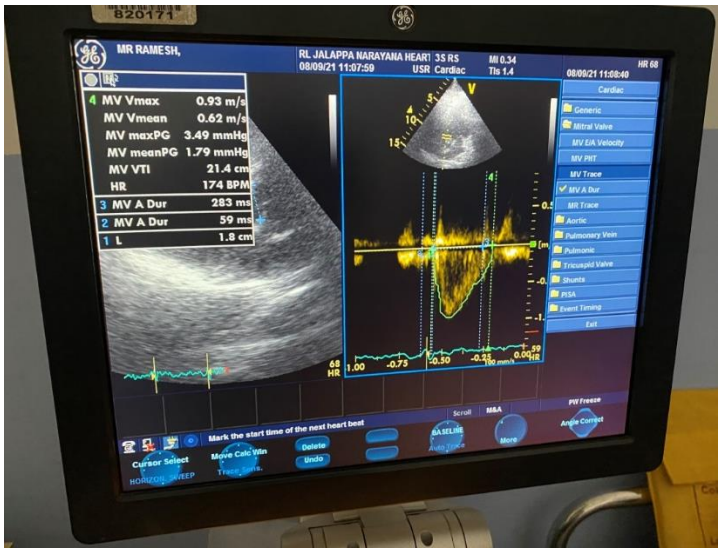



***Fig 9.*** *Assessment of Stroke volume.*

**Heart rate variability measurements**

Fifteen minutes short-term HRV indices were measured[33] (using 4-Channel PowerLab15T Data acquisition software) using lead II electrocardiogram. For all the recruited subjects, HRV measurements were done with the negative electrode on the right 2$^{nd}$ intercostal space (ICS) in the mid-clavicular line (MCL), with the positive electrode on the left 5$^{th}$ ICS in the MCL, and the ground electrode on left 2$^{nd}$ ICS in MCL with the patient in the supine position for 5-10 min. Heart rate variability[33] was analyzed using LabChart 7.3.8 data analysis software and MLS310 HRV module developed by AD Instruments, Australia.

Accordingly, time domain parameters[33] measured was as follows:

**SDNN (ms)**: Is the root mean square deviation of the N-N intervals.

**rMSSD (ms)**: Is the square root of the mean squared differences of successive NN intervals.

Further, frequency domain parameters[33] measured were:

**Total power (TP) ($ms^2$)**: Indicates the overall heart rate variability.

**Low frequency (LF) power ($ms^2$)**: concerned with both sympathetic and parasympathetic activity. Predominantly related to sympathetic nervous system activity.

**High Frequency (HF) power ($ms^2$)**: Indicates parasympathetic activity.

**Low-frequency (LF norm/LFnu) and High-frequency (HF norm/HFnu) in normalized units**: This emphasizes the balance between the parasympathetic and sympathetic arms.

HF norm= HF/ (TP-VLF)*100 => HF/ (LF+HF)*100

LF norm= LF/ (TP-VLF)*100 => LF/ (LF+HF)*100

**LF/HF ratio**: Denotes Sympathovagal balance.

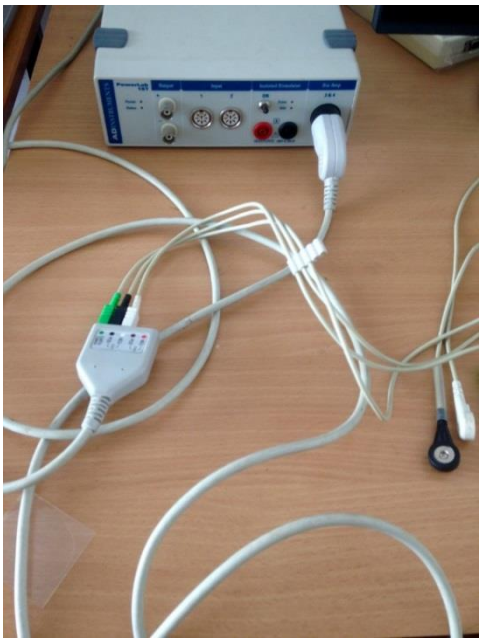


***Fig 10a.*** *ADInstruments PowerLab 15T*

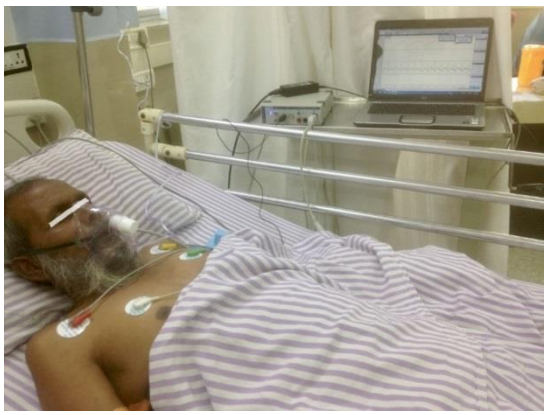


***Fig 10b.*** *On admission/baseline Heart rate variability measurement at Coronary care unit.*

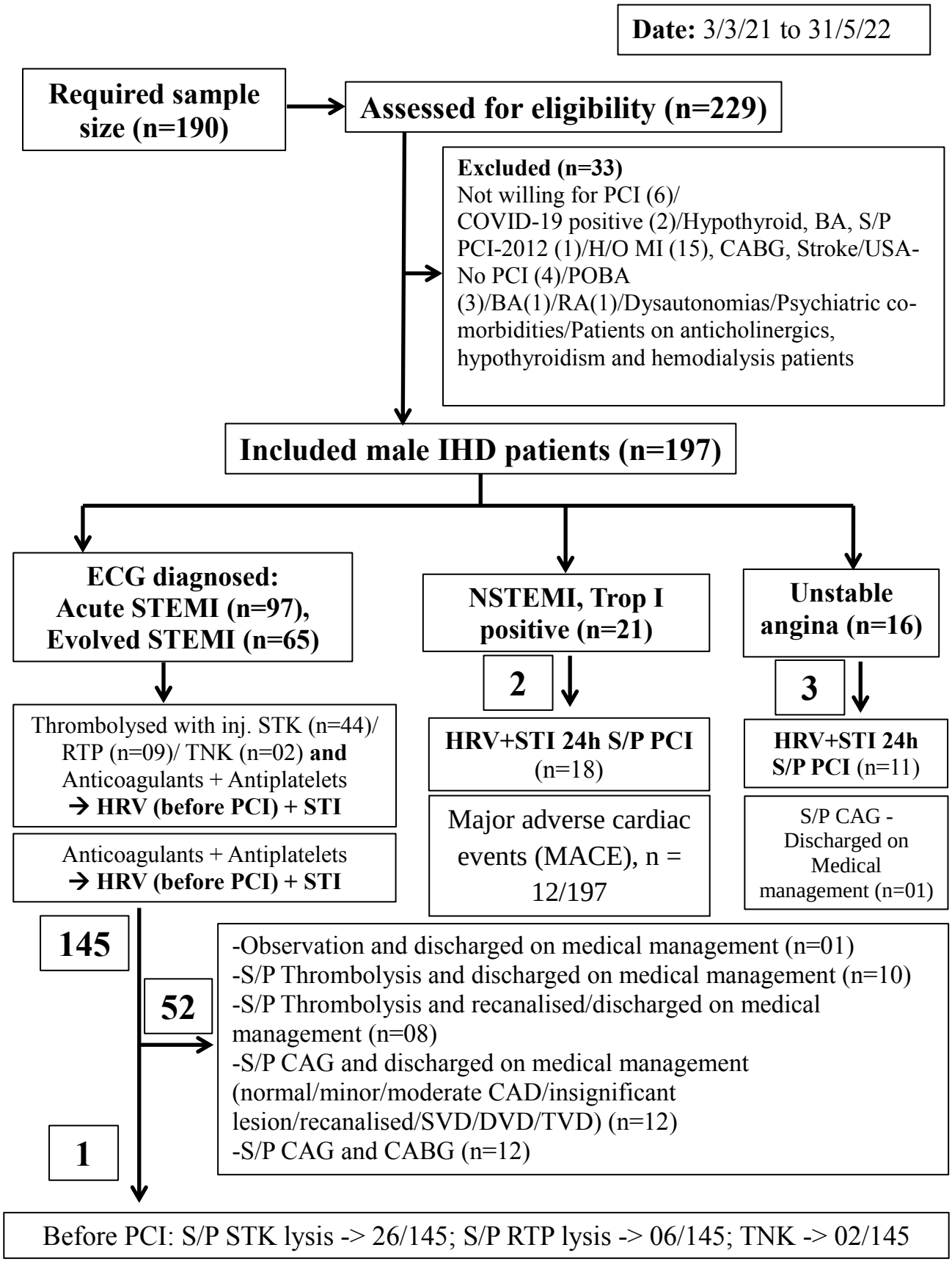

***Fig 10c.*** *24h post-PCI Heart rate variability measurement at ward.*

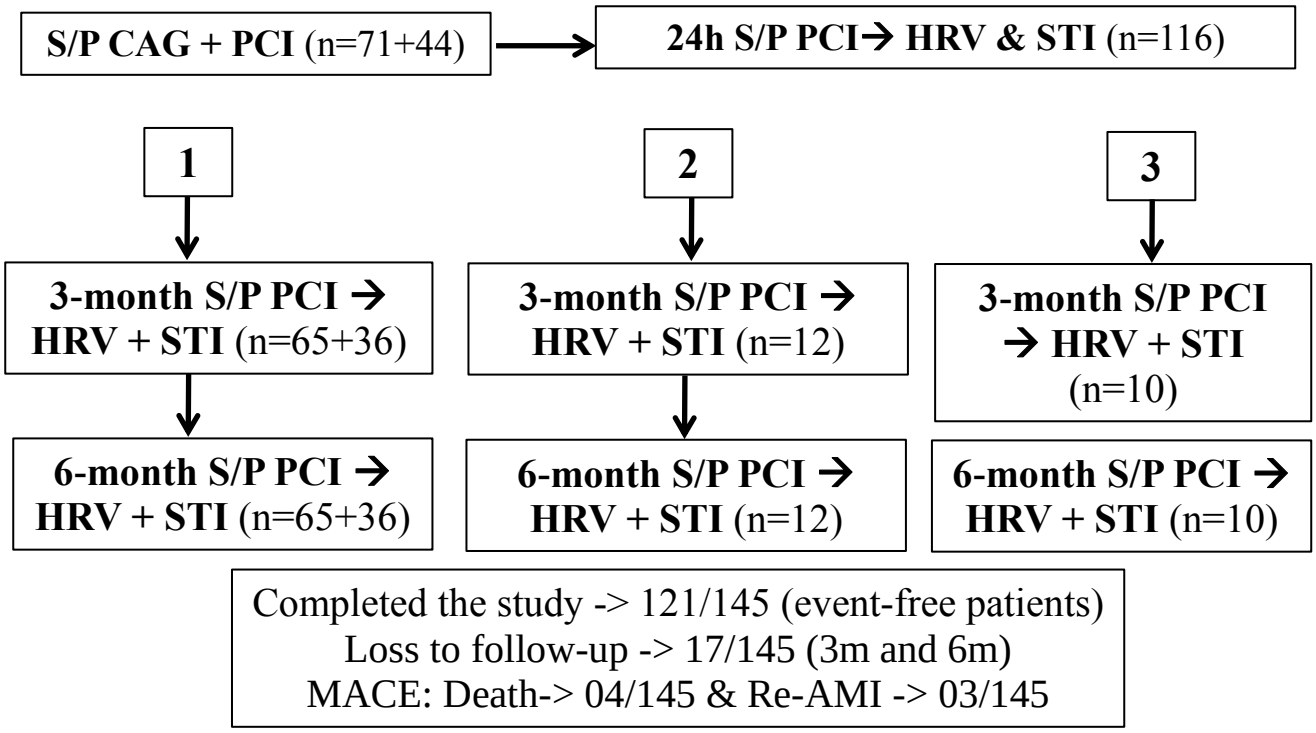
***Fig 10d.*** *3- or 6-month post-PCI Heart rate variability measurement at Cardiology OPD*

**Health-related Quality of Life assessment:**

Patients' quality of life has been investigated using the Short Form-12 health survey questionnaire.[45, 58] Accordingly, face-to-face interviews were conducted at Cardiology OPD at various time points. Consequently, PCS-12 and MCS-12 scores were measured 1-month post-PCI/post-phase 2 cardiac rehabilitation, 3-, and 6-month post-PCI.

***Study flow for recruiting IHD patients and procuring STI and HRV indices:***






1. Major adverse cardiac events (MACE) -> Death or re-AMI -> 12/197
2. **Death** of 08/197 IHD patients recorded **within 30 days of follow-up** and01/44 Evolved MI patient died **within 3 months S/P PCI.**
3. 3 Patients had Re-AMI (01 AMI-> AMI), (1 EMI-> Recent MI) & (1 EMI -> NSTEMI). One Patient had thrombolysis (Inj. STK) and 2 Patients had Re-PCI
4. Event-free baseline Patients, n=185

## STATISTICAL ANALYSIS

Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. All quantitative variables were measured and compared using independent t-test and two-way repeated measures ANOVA and stated as mean ± SD. Chi-square or Fisher exact test was used to measure the categorical variables. Pearson correlation analysis was used to find out the relationship between the STI and HRV. Pearson correlations was executed to find out the link between the body mass index with STI and HRV. Pearson's correlation analysis was done to correlate quality of life in post-PCI patients with the STI and HRV. Multivariate regression analyses were done to know the association of risk factors with STI and HRV. The HRV cut-off values were defined by the Receiver Operating Characteristic (ROC) curve. The sensitivity and specificity values were also determined. An area under the curve ≥0.650 was considered significant. (**Pivatelli *et al.* 2012**) Level of statistical significance was set at $p \leq 0.05$. For the data analysis, SPSS version 22.0 (SPSS Inc., Chicago, IL) statistical software was utilised. Microsoft excel and SPSS software's were used to generate graphs.

# *RESULTS*

# RESULTS

The study population comprised of 197 male IHD patients (Killip Class I to IV) [37] with acute or evolved myocardial infarction (n=181) and unstable angina (n=16) admitted at CCU, between March and November 2021. Among the included, 50.43% IHD patients had anterior wall myocardial infarction. Among them, 189 (95.9%) patients had angina and 23 (11.7%) patients had dyspnea. Patients who smoked cigarette/beedi, [29, 58] (n=63; 31.98 %) tobacco chewers (n=08; 4.06 %), and alcoholics[54] (n=37; 18.78 %) were also included in the study. Among the included, 35.53 % (n=70) of them were diabetics and 36.55% (n=72) of them were hypertensive. Patients on diuretics[57] (n=116; 58.88%) were also allowed to participate in the present study. Thirty-one patients (22%) received thrombolytic therapy with streptokinase (15000 UI/hour) or reteplase or tenecteplase. In addition, 79 patients (54.50%) underwent primary PCI within 12-24h from the chest pain onset, 65 patients went through elective PCI (45%), rescue PCI was done in an IHD patient and was associated with procedural success in all. All the recruited patients were COVID-19 negative. None of the recruited had atrial fibrillation. The On admission details of the study population are given in **Table 1.**

**Table 1.** On admission attributes of ischemic heart disease patients (n=197)

| **Characteristics** | **Mean ± SD** |
|---|---|
| Mean age (years) | 54.09 ± 11.75 |
| BMI ($Kg/m^2$) | 25.2 ± 33.93 |
| Glucose random blood sugar (mg/dl) | 170.61 ± 74.35 |
| **Myocardial necrosis markers (n)** | |
| Troponin I (ng/ml), (n=54) | Positive (44) |
| Creatine Kinase-MB (ng/ml), (n=39) | Abnormal (27) |

| | |
|---|---|
| **Culprit Coronary vessels with significant lesions (>50%)** | |
| Single vessel disease | 87 |
| Double vessel disease | 36 |
| Triple vessel disease | 15 |
| **TIMI flow Grade III (post-PCI)** | 145 |

*TIMI: Thrombolysis in myocardial infarction; BMI: Body mass index*

2D-Echocardiographic parameters on admission are given in **Table 2.**

**Table 2:** Baseline 2D-Echocardiographic parameters

| **VARIABLES** | **No. of patients (n=197)** | **%** |
|---|---|---|
| Stroke volume (ml) | | |
| • <50 | 73 | 37.1 |
| • 50-60 | 110 | 55.8 |
| • >60 | 14 | 7.1 |
| Regional wall motion abnormality | | |
| • No | 27 | 13.7 |
| • Yes | 170 | 86.3 |
| Left ventricular hypertrophy (LVH) | | |
| • Concentric LVH (≥13 mm) | 40 | 20.3 |
| • Hypertrophied LVH | 2 | 1.0 |
| • Mild concentric LVH (≤12 mm) | 13 | 6.6 |
| • No LVH (6-9 mm) | 142 | 72.1 |
| Mitral regurgitation | | |
| • Mild | 152 | 77.2 |
| • Moderate | 28 | 14.2 |
| • Severe | 4 | 2.0 |
| • Trivial | 13 | 6.6 |
| Aortic stenosis | | |

| | | |
|---|---|---|
| • No | 192 | 97.5 |
| • Sclerotic | 5 | 2.5 |
| Aortic regurgitation | | |
| • Mild | 113 | 57.4 |
| • Trivial | 84 | 42.6 |
| LV systolic dysfunction (LVSD) | | |
| • Normal LV systolic function | 30 | 15.2 |
| • Mild LVSD | 82 | 41.6 |
| • Moderate LVSD | 35 | 17.8 |
| • Preserved LV systolic function | 23 | 11.7 |
| • Adequate LV systolic function | 18 | 9.1 |
| • Severe LVSD | 7 | 3.6 |
| • Moderate to severe LVSD | 2 | 1.0 |
| LV diastolic dysfunction (LVDD) | | |
| • Normal LV diastolic function | 144 | 73.1 |
| • GRADE I LVDD | 48 | 24.4 |
| • GRADE II LVDD | 3 | 1.5 |
| • GRADE III LVDD | 2 | 1.0 |
| CLOT/VEG/ Pericardial effusion (P.E.) | | |
| • No | 191 | 97.0 |
| • Yes | 6 | 3.0 |
| I. LV apical Clot + | 4 | 2.0 |
| II. LV apical clot ++ | 1 | 0.5 |
| III. P.E. | 1 | 0.5 |
| LVEF% | | |
| • <40 | 46 | 23.4 |
| • 40-50 | 104 | 52.8 |
| • >50 | 47 | 23.9 |
| Ventricular tachycardia | | |
| • Absent | 191 | 97.0 |
| • Present | 6 | 3.0 |

***OBJECTIVE 1. To estimate systolic time intervals (STI) and heart rate variability (HRV) among ischemic heart disease patients before percutaneous coronary intervention (PCI), 24 hours post-PCI, 3- and 6 months post-PCI.***

With the 2D-echocardiography, STIs recorded are presented in **Table 3**.

**Table 3.** Systolic time intervals of IHD patients on admission, 24h-, 3-, and 6-month post-PCI (n=197)

| STI values | Total |
|---|---|
| PEP (ms) | |
| • Baseline | 90.99±27.98 |
| • 24h post-PCI | 90.67±26.86 |
| • 3-month post-PCI | 87.34±21.01 |
| • 6-month post-PCI | 85.70±16.65 |
| LVET (ms) | |
| • Baseline | 279.15±44.55 |
| • 24h post-PCI | 285.54±41.71 |
| • 3-month post-PCI | 285.12±41.88 |
| • 6-month post-PCI | 285.90±37.71 |
| $QS_2$ (ms) | |
| • Baseline | 370.14±48.84 |
| • 24h post-PCI | 376.21±43.55 |
| • 3-month post-PCI | 372.47±44.52 |
| • 6-month post-PCI | 371.37±40.19 |
| PEP/LVET | |
| • Baseline | 0.34±0.13 |
| • 24h post-PCI | 0.33±0.13 |
| • 3-month post-PCI | 0.31±0.10 |
| • 6-month post-PCI | 0.31±0.08 |

Heart rate variability values are presented in **Table 4.**

**Table 4.** Heart rate variability and heart rate values of IHD patients on admission, 24h-, 3-, and 6-month post-PCI (n=197).

| **HRV indices** | **Total** |
|---|---|
| SDNN (ms) | |
| • Baseline | 47.27±32.43 |
| • 24h post-PCI | 38.39±27.61 |
| • 3 month post-PCI | 40.75±21.63 |
| • 6 month post-PCI | 42.56±21.84 |
| rMSSD (ms) | |
| • Baseline | 51.42±47.42 |
| • 24h post-PCI | 41.39±45.87 |
| • 3 month post-PCI | 44.38±33.38 |
| • 6 month post-PCI | 45.09±32.46 |
| TP ($ms^2$) | |
| • Baseline | 3076.18±4908.54 |
| • 24h post-PCI | 2166.69±4847.86 |
| • 3 month post-PCI | 2057.45±2004.86 |
| • 6 month post-PCI | 2203.69±2032.97 |
| LF ($ms^2$) | |
| • Baseline | 555.37±1068.68 |
| • 24h post-PCI | 305.99±496.83 |
| • 3-month post-PCI | 358.63±426.67 |
| • 6-month post-PCI | 384.14±431.54 |
| HF ($ms^2$) | |

| | |
|---|---|
| • Baseline | 746.65±1571.34 |
| • 24h post-PCI | 459.20±984.47 |
| • 3-month post-PCI | 543.79±684.79 |
| • 6-month post-PCI | 521.29±619.12 |
| LFnu | |
| • Baseline | 38.81±25.64 |
| • 24h post-PCI | 40.96±27.45 |
| • 3-month post-PCI | 36.40±22.23 |
| • 6-month post-PCI | 35.27±19.57 |
| HFnu | |
| • Baseline | 28.46±13.85 |
| • 24h post-PCI | 27.54±14.47 |
| • 3-month post-PCI | 34.17±13.02 |
| • 6-month post-PCI | 34.31±11.00 |
| LF/HF ratio | |
| • Baseline | 2.24±2.94 |
| • 24h post-PCI | 2.80±4.25 |
| • 3-month post-PCI | 1.32±1.37 |
| • 6-month post-PCI | 1.13±0.83 |
| Heart Rate (bpm) | |
| • Baseline | 84.83±14.71 |
| • 24h post-PCI | 85.38±13.51 |
| • 3-month post-PCI | 81.12±13.26 |
| • 6-month post-PCI | 80.65±12.52 |

***OBJECTIVE 2.1. To estimate the occurrence of Major adverse cardiac events (MACE)***

In the current study, at a follow-up of 6 months, out of 197 IHD patients, major adverse cardiac events (MACE) occurred in 12 patients (6.1%) (Cardiac death was 1.5%, while that of sudden death was 4.5%). Out of twelve-MACE, nine deaths and three re-AMIs occurred (**Table 5**). Furthermore, at a follow-up of 6 months, out of 145 IHD patients who underwent PCI, MACE occurred in 07 patients (4.8%) (Cardiac death was 2.1%, while that of sudden death was 2.75%). Out of seven-MACE, four deaths and three re-AMIs occurred.

**Table 5.** Frequency distribution of IHD patients studied based on Major adverse cardiac events (MACE).

| **MACE** | **No. of patients (n=197)** | **%** |
|---|---|---|
| No | 185 | 93.9 |
| Yes | 12 | 6.1 |
| Total | 197 | 100.0 |

***OBJECTIVE 2.2. To estimate the STI and HRV in IHD patients with and without major adverse cardiac events (MACE)***

An independent t-test was performed to compare the STI values in patients with and without MACE. A statistically significant difference between baseline PEP and PEP/LVET were found between patients who had MACE and without MACE. **Table 6** shows the baseline/on admission STIs in IHD patients with and without MACE.

**Table 6.** Comparison of Baseline Systolic time intervals between IHD patients with and without MACE using Independent t-test

| **Baseline Systolic time intervals** | **MACE** | | ***P* value** |
|---|---|---|---|
| | **No** | **Yes** | |
| PEP | 89.63±26.87 | 112.08±36.81 | **0.007**** |
| LVET | 279.77±44.72 | 269.50±42.46 | $0.440^{NS}$ |
| $QS_2$ | 369.4±47.80 | 381.58±64.30 | $0.404^{NS}$ |
| PEP/LVET | 0.33±0.13 | 0.42±0.13 | **0.027*** |

****** Moderately significant p ≤0.05; ** Strongly significant p ≤0.01; NS: Not significant.***

An independent t-test was performed to compare the HRV variables in patients with and without MACE. There was a statistically significant difference between baseline SDNN, rMSSD, TP, and HF HRV indices in patients who had MACE and without MACE. **Table 7** shows the on admission HRV values in IHD patients with and without MACE.

**Table 7.** Comparison of baseline heart rate variability parameters between IHD patients with and without MACE using Independent t-test

| **Baseline HRV parameters** | **MACE** | | ***P* value** |
|---|---|---|---|
| | **No** | **Yes** | |
| SDNN | 46.01±30.61 | 66.6±51.33 | **0.033*** |
| rMSSD | 49.42±44.29 | 82.24±78.44 | **0.020*** |
| TP | 2866.33±4437.06 | 6311.25±9371.89 | **0.018*** |
| LF | 533.58±985.17 | 891.42±1995.93 | 0.262 |
| HF | 664.31±1378.71 | 2015.98±3213.69 | **0.004**** |
| LFnu | 39.30±25.51 | 31.30±27.58 | 0.297 |
| HFnu | 28.09±13.67 | 34.15±15.94 | 0.143 |
| LF/HF | 2.28±2.99 | 1.56±2.04 | 0.412 |
| HR | 85.19±14.65 | 79.28±15.15 | 0.178 |

***** *Moderately significant p ≤0.05; ** Strongly significant p ≤0.01; NS: Not significant.*

***OBJECTIVE 2.3. To evaluate STI among IHD patients with and without major adverse cardiac events (MACE).***

A two-way repeated measure ANOVA was performed to know the effect of percutaneous coronary intervention systolic time intervals in IHD patients over the time (**Table 8)**. The PEP ($p$<0.001) and PEP/LVET ($p$=0.008) ratios before and after PCI differed significantly.

**Table 8.** Comparison of Systolic time intervals between IHD patients with and without MACE on admission/baseline, 24h-, 3-, and 6-month post-PCI using two-way repeated measures ANOVA

| STI values | MACE | | *P* value | 2X4 Repeated ANOVA |
|---|---|---|---|---|
| | No | Yes | | |
| PEP | | | | |
| • Baseline | 89.63±26.87 | 112.08±36.81 | **0.007**$^{**}$ | Group F=5.172, ***P*=0.025**$^{*}$; Time F=7.426, ***p*<0.001**$^{**}$ |
| • 24h post-PCI | 89.97±26.36 | 103.43±34.75 | 0.198$^{NS}$ | |
| • 3-month post-PCI | 87.12±20.29 | 95.67±47.06 | 0.489$^{NS}$ | |
| • 6-month post-PCI | 85.36±16.49 | 98.33±21.73 | 0.184$^{NS}$ | |
| LVET | | | | |
| • Baseline | 279.77±44.72 | 269.50±42.46 | 0.440$^{NS}$ | Group F=1.898, *P*=0.171$^{NS}$; Time F=0.183, *p*=0.908$^{NS}$ |
| • 24h post-PCI | 284.88±42.46 | 297.71±22.85 | 0.430$^{NS}$ | |
| • 3-month post-PCI | 284.21±41.96 | 319.33±21.39 | 0.153$^{NS}$ | |
| • 6-month post-PCI | 285.33±37.77 | 307.33±34.39 | 0.321$^{NS}$ | |
| $QS_2$ | | | | |
| • Baseline | 369.40±47.80 | 381.58±64.30 | 0.404$^{NS}$ | Group F=6.597, ***P*=0.012**$^{*}$ Time F=1.157, *p*=0.326$^{NS}$ |
| • 24h post-PCI | 374.84±43.54 | 401.14±38.08 | 0.120$^{NS}$ | |
| • 3-month post-PCI | 371.34±44.24 | 415.00±40.04 | 0.094$^{+}$ | |
| • 6-month post-PCI | 370.46±39.93 | 405.67±42.52 | 0.135$^{NS}$ | |
| PEP/LVET | | | | |
| • Baseline | 0.33±0.13 | 0.42±0.13 | **0.027**$^{*}$ | Group F=0.913, *P*=0.341$^{NS}$ |
| • 24h post-PCI | 0.33±0.13 | 0.35±0.12 | 0.641$^{NS}$ | |

| | | | | |
|---|---|---|---|---|
| • 3-month post-PCI | 0.31±0.10 | 0.31±0.17 | 0.889$^{NS}$ | Time F=4.024, ***p*=0.008**$^{**}$ |
| • 6-month post-PCI | 0.31±0.08 | 0.32±0.08 | 0.758$^{NS}$ | |

**Moderately significant p ≤0.05; + suggestive significance (P value: 0.05<p<0.10); NS: Not significant; PEP: Pre-ejection period; LVET: Left ventricular ejection time; $QS_2$: Total electro-mechanical systole.*

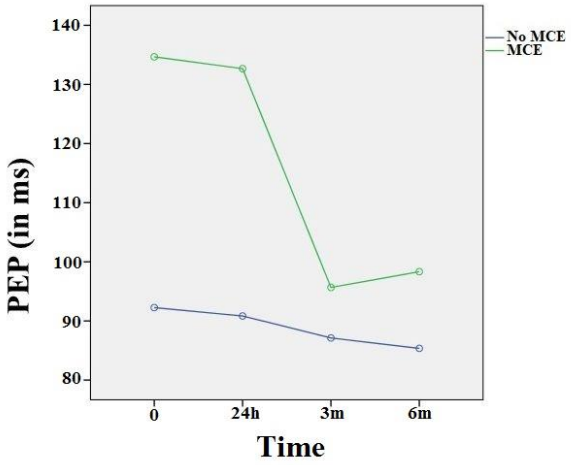



***Fig 11a.*** *Pre-ejection period (PEP) measured at baseline, 24h, 3-, and 6-month post-PCI.*

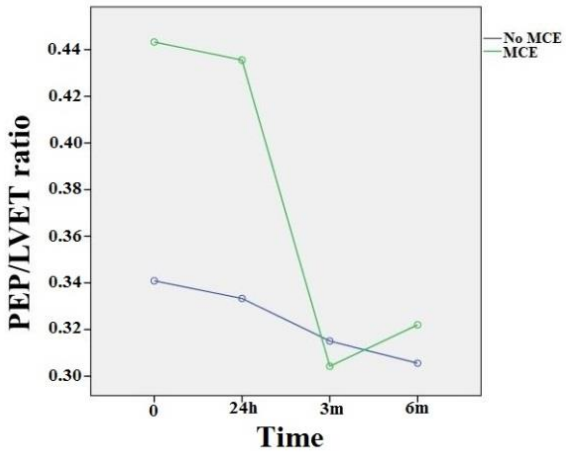



***Fig 11b.*** *PEP/LVET ratios at baseline, 24h, 3-, and 6-month post-PCI.*

Bonferroni post-hoc test for pairwise comparisons found that the mean value of PEP STI was significantly different between [(Baseline) and (3-month post-PCI)] ($p$ = 0.014; 95% C.I. = 2.991 to 41.142); [(Baseline) and (6-month post-PCI)] ($p$ = 0.032; 95% C.I. = 1.146 to 42.081). Furthermore, the mean value of PEP STI was significantly different between [24h

post-PCI] and [3-month post-PCI] ($p$ = 0.009; 95% C.I. = 3.608 to 37.108); between [24h post-PCI] and [3-month post-PCI] ($p$ = 0.030; 95% C.I. = 1.233 to 38.578) respectively.

**Table.** Pairwise comparisons of pre- and post-PCI *PEP* STI using Bonferroni Post Hoc test (n=116)

| Time (I) | Time (J) | Mean Difference (I-J) | Std. Error | Sig.[b] | 95% CI[b] | |
|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound |
| **Baseline** | **24h** | 1.708 | 5.292 | 1.000 | -12.500 | 15.916 |
| | **3m** | 22.066* | 7.104 | **0.014*** | 2.991 | 41.142 |
| | **6m** | 21.614* | 7.623 | **0.032*** | 1.146 | 42.081 |
| **24h post-PCI** | **Baseline** | -1.708 | 5.292 | 1.000 | -15.916 | 12.500 |
| | **3m** | 20.358* | 6.238 | **0.009*** | 3.608 | 37.108 |
| | **6m** | 19.906* | 6.954 | **0.030*** | 1.233 | 38.578 |
| **3m post-PCI** | **Baseline** | -22.066* | 7.104 | 0.014 | -41.142 | -2.991 |
| | **24h** | -20.358* | 6.238 | 0.009 | -37.108 | -3.608 |
| | **6m** | -0.453 | 3.771 | 1.000 | -10.579 | 9.673 |
| **6m post-PCI** | **Baseline** | -21.614* | 7.623 | 0.032 | -42.081 | -1.146 |
| | **24h** | -19.906* | 6.954 | 0.030 | -38.578 | -1.233 |
| | **3m** | 0.453 | 3.771 | 1.000 | -9.673 | 10.579 |

**The mean difference is significant at p ≤0.05 level; b. Adjustment for multiple comparisons: Bonferroni; CI: Confidence interval*

***OBJECTIVE 2.4. To evaluate HRV among IHD patients with and without major adverse cardiac events (MACE).***

A two-way repeated measures ANOVA was performed to know effect of PCI on HRV among IHD patients over the time (**Table 9**). It revealed that a large disparity existed between the pre- and post-PCI time- (SDNN, rMSSD) and frequency-domain (HF, LFnu, HFnu, and LF/HF ratio) HRV indices. In addition, the heart rate before and after PCI differed significantly. A statistically significant difference between 24h post-PCI SDNN, rMSSD, TP,

and HF HRV indices were also found. In addition, there existed a statistically significant alteration between baselines, 24h after PCI, and 3-month post-PCI heart rate between patients with and without MACE.

**Table 9.** Comparison of Heart rate variability measures between IHD patients with or without MACE using independent t-test. HRV measures at baseline, 24h post-PCI, 3-, and 6-month post-PCI using two-way repeated measures ANOVA.

| **HRV indices** | **MACE** | | ***P* value** | **2X4 Repeated ANOVA** |
|---|---|---|---|---|
| | **No** | **Yes** | | |
| SDNN | | | | |
| • Baseline | 46.01±30.61 | 66.60±51.33 | **0.033*** | Group F=0.150, P=0.699; Time F=2.810, ***p*=0.040*** |
| • 24h post-PCI | 36.44±22.00 | 74.00±72.25 | **<0.001*** | |
| • 3 month post-PCI | 41.09±21.8 | 27.90±6.51 | 0.299NS | |
| • 6 month post-PCI | 42.51±21.97 | 44.43±19.82 | 0.881NS | |
| rMSSD | | | | |
| • Baseline | 49.42±44.29 | 82.24±78.44 | **0.020*** | Group F=0.034, P=0.853; Time F=2.676, ***p*=0.047*** |
| • 24h post-PCI | 38.04±33.64 | 102.69±135.73 | **<0.001*** | |
| • 3 month post-PCI | 44.70±33.62 | 32.33±23.23 | 0.529NS | |
| • 6 month post-PCI | 44.87±32.42 | 53.31±40.46 | 0.659NS | |
| TP | | | | |
| • Baseline | 2866.33±4437.06 | 6311.25±9371.89 | **0.018*** | Group |

| | | | | |
|---|---|---|---|---|
| • 24h post-PCI | 1733.06±1880.50 | 10095.81±19304.44 | **<0.001**** | F=0.060, P=0.807; Time F=1.869, p=0.134$^{NS}$ |
| • 3 month post-PCI | 2086.54±2020.64 | 961.71±788.81 | 0.340$^{NS}$ | |
| • 6 month post-PCI | 2199.94±2037.15 | 2345.21±2284.01 | 0.903$^{NS}$ | |
| LF | | | | |
| • Baseline | 533.58±985.17 | 891.42±1995.93 | 0.262$^{NS}$ | Group F=0.384, P=0.537; Time F=0.317, p=0.813$^{NS}$ |
| • 24h post-PCI | 264.39±347.40 | 1066.79±1498.67 | **<0.001**** | |
| • 3-month post-PCI | 365.23±430.32 | 109.98±53.78 | 0.309$^{NS}$ | |
| • 6-month post-PCI | 381.71±433.13 | 475.84±435.53 | 0.711$^{NS}$ | |
| HF | | | | |
| • Baseline | 664.31±1378.71 | 2015.98±3213.69 | **0.004**** | Group F=0.307, P=0.581; Time F=3.648, ***p*=0.013*** |
| • 24h post-PCI | 362.97±517.13 | 2218.76±3489.25 | **<0.001**** | |
| • 3-month post-PCI | 548.88±691.13 | 352.15±398.45 | 0.625$^{NS}$ | |
| • 6-month post-PCI | 516.09±616.25 | 717.12±845.14 | 0.581$^{NS}$ | |
| LFnu | | | | |
| • Baseline | 39.30±25.51 | 31.30±27.58 | 0.297$^{NS}$ | Group F=0.291, P=0.590; Time F=3.622, ***p*=0.013*** |
| • 24h post-PCI | 41.13±27.02 | 37.96±36.85 | 0.768$^{NS}$ | |
| • 3-month post-PCI | 36.39±22.15 | 36.76±30.55 | 0.977$^{NS}$ | |

| | | | | |
|---|---|---|---|---|
| • 6-month post-PCI | 35.22±19.73 | 37.18±14.52 | 0.865$^{NS}$ | |
| HFnu | | | | |
| • Baseline | 28.09±13.67 | 34.15±15.94 | 0.143$^{NS}$ | Group F=0.156, P=0.694; Time F=5.679, *p*=0.001** |
| • 24h post-PCI | 27.49±14.36 | 28.45±17.51 | 0.865$^{NS}$ | |
| • 3-month post-PCI | 33.96±13.04 | 41.9±11.77 | 0.299$^{NS}$ | |
| • 6-month post-PCI | 34.09±11.01 | 42.68±7.50 | 0.183$^{NS}$ | |
| LF/HF ratio | | | | |
| • Baseline | 2.28±2.99 | 1.56±2.04 | 0.412$^{NS}$ | Group F=1.710, P=0.194; Time F=9.177, ***p*<0.001**$^{**}$ |
| • 24h post-PCI | 2.74±4.17 | 3.86±5.86 | 0.498$^{NS}$ | |
| • 3-month post-PCI | 1.33±1.38 | 1.03±1.08 | 0.713$^{NS}$ | |
| • 6-month post-PCI | 1.13±0.84 | 0.85±0.25 | 0.567$^{NS}$ | |
| Heart Rate | | | | |
| • Baseline | 85.19±14.65 | 79.28±15.15 | 0.178$^{NS}$ | Group F=2.709, P=0.103; Time F=3.788, ***p*=0.011**$^{*}$ |
| • 24h post-PCI | 85.92±13.47 | 75.43±10.56 | **0.045*** | |
| • 3-month post-PCI | 81.53±13.19 | 65.67±0.58 | **0.040**$^{*}$ | |
| • 6-month post-PCI | 80.95±12.52 | 69.33±5.77 | 0.113$^{NS}$ | |

** Moderately Significant p ≤0.05; ** Strongly significant p ≤0.01; NS: Not significant; SDNN: N-N intervals standard deviation; rMSSD: consecutive N-N interval disparities' root mean square; TP:*

*Total power; LF: Low-frequency; HF: High-frequency; LFnu: Low-frequency normalized unit; HF-nu: High-frequency normalized unit.*

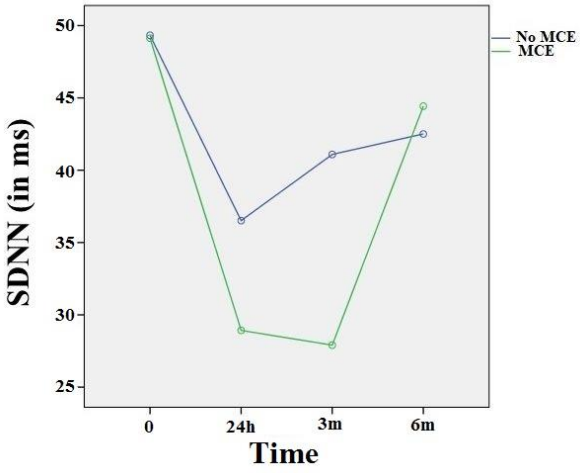



***Fig 12a.*** *Standard deviation of N-N intervals. (SDNN) at baseline, 24h, 3-, and 6-month post-PCI.*

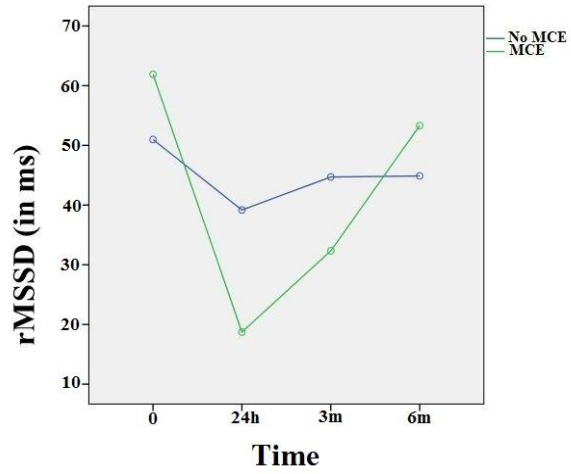



***Fig 12b.*** *Square root of the mean squared differences of successive N-N intervals (rMSSD) at baseline, 24h, 3-, and 6-month post-PCI.*

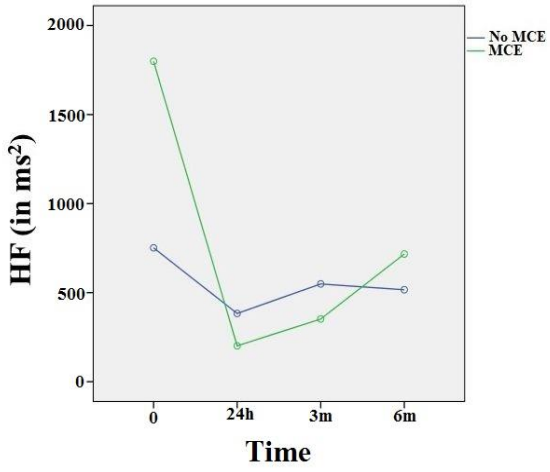


***Fig 12c.*** *High-frequency power (HF) at baseline, 24h, 3-, and 6-month post-PCI*

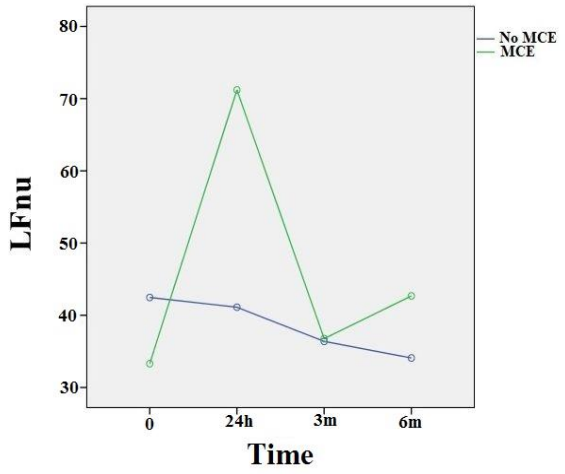



***Fig 12d.*** *Low-frequency normalized unit (LFnu) at baseline, 24h, 3-, and 6-month post-PCI*

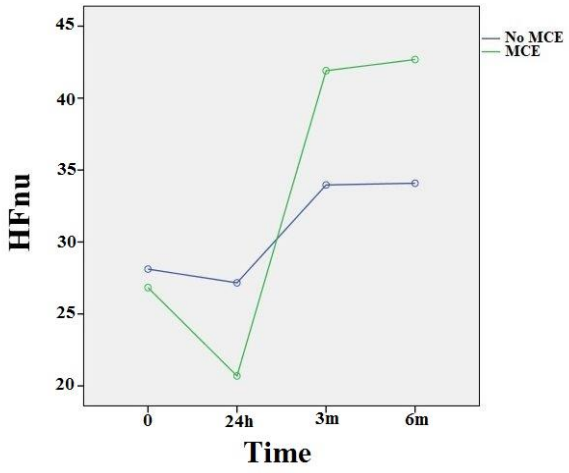



***Fig 12e.*** *High-frequency normalized unit (HFnu) at baseline, 24h, 3-, and 6-month post-PCI*

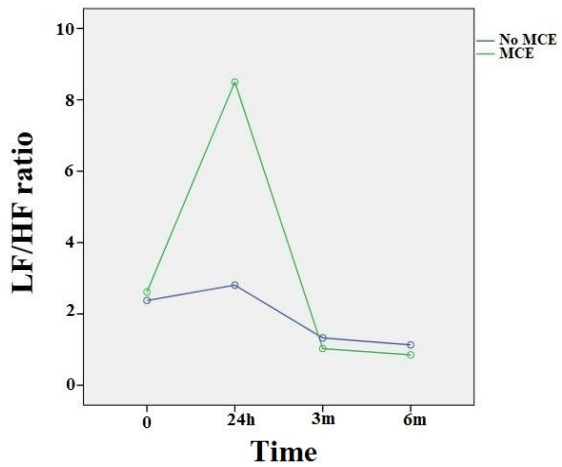



***Fig 12f.*** *LF/HF ratio at baseline, 24h, 3-, and 6-month post-PCI*

Bonferroni post-hoc test for pairwise comparisons found that the mean value of SDNN HRV index was significantly different between (3 month post-PCI) and (6 month post-PCI) [$p$ = 0.025; 95% C.I. = -17.215 to -0.731]. Furthermore, the mean value of HFnu HRV index was significantly different between [24h post-PCI] and [3-month post-PCI] ($p$ = 0.023; 95% C.I. = -26.717 to -1.294); between [24h post-PCI] and [3 month post-PCI] ($p$ = 0.011; 95% C.I. = -26.604 to -2.308) respectively.

**Table.** Pairwise comparisons of pre- and post-PCI *SDNN* HRV index using Bonferroni Post Hoc test (n=116).

| Time (I) | Time (J) | Mean Difference (I-J) | Std. Error | Sig.[b] | 95% CI[b] | |
|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound |
| **Baseline** | **24h** | 16.505 | 8.460 | 0.321 | -6.212 | 39.221 |
| | **3m** | 14.728 | 7.938 | 0.397 | -6.587 | 36.043 |
| | **6m** | 5.755 | 7.561 | 1.000 | -14.547 | 26.056 |
| **24h post-PCI** | **Baseline** | -16.505 | 8.460 | 0.321 | -39.221 | 6.212 |
| | **3m** | -1.777 | 5.390 | 1.000 | -16.251 | 12.696 |
| | **6m** | -10.750 | 5.158 | 0.236 | -24.599 | 3.099 |
| **3m post-PCI** | **Baseline** | -14.728 | 7.938 | 0.397 | -36.043 | 6.587 |
| | **24h** | 1.777 | 5.390 | 1.000 | -12.696 | 16.251 |
| | **6m** | -8.973* | 3.069 | **0.025*** | -17.215 | -0.731 |
| **6m post-PCI** | **Baseline** | -5.755 | 7.561 | 1.000 | -26.056 | 14.547 |
| | **24h** | 10.750 | 5.158 | 0.236 | -3.099 | 24.599 |
| | **3m** | 8.973* | 3.069 | 0.025* | 0.731 | 17.215 |

** the mean difference is significant at p ≤0.05 level; b. Adjustment for multiple comparisons: Bonferroni.*

**Table.** Pairwise comparisons of pre- and post-PCI *HFnu* HRV index using Bonferroni Post Hoc test (n=116).

| Time (I) | Time (J) | Mean Difference (I-J) | Std. Error | Sig.[b] | 95% CI[b] | |
|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound |
| **Baseline** | **24h** | 3.547 | 4.595 | 1.000 | -8.791 | 15.886 |
| | **3m** | -10.458 | 4.664 | 0.161 | -22.981 | 2.065 |
| | **6m** | -10.908 | 4.217 | 0.066 | -22.231 | 0.414 |
| **24h post-PCI** | **Baseline** | -3.547 | 4.595 | 1.000 | -15.886 | 8.791 |
| | **3m** | -14.006* | 4.734 | **0.023*** | -26.717 | -1.294 |
| | **6m** | -14.456* | 4.524 | **0.011*** | -26.604 | -2.308 |
| **3m post-PCI** | **Baseline** | 10.458 | 4.664 | 0.161 | -2.065 | 22.981 |
| | **24h** | 14.006* | 4.734 | 0.023* | 1.294 | 26.717 |
| | **6m** | -0.450 | 3.198 | 1.000 | -9.037 | 8.137 |
| **6m post-PCI** | **Baseline** | 10.908 | 4.217 | 0.066 | -0.414 | 22.231 |
| | **24h** | 14.456* | 4.524 | 0.011* | 2.308 | 26.604 |
| | **3m** | 0.450 | 3.198 | 1.000 | -8.137 | 9.037 |

**The mean difference is significant at p ≤0.05 level; b. Adjustment for multiple comparisons: Bonferroni; CI: Confidence interval*

***OBJECTIVE 3. To correlate STI with the measures of HRV among IHD patients.***

Pearson's correlations were implemented to discriminate the credible correlation between baseline systolic time intervals and HRV parameters among IHD patients without MACE. Baseline STIs which had significant positive correlations with the HRV indices were [SDNN vs. PEP ($p$ = 0.034); rMSSD vs. PEP ($p$ = 0.022); HF vs. PEP ($p$ = 0.044); HFnu vs. LVET ($p$ = 0.035); SDNN vs. $QS_2$ ($p$ = 0.010); rMSSD vs. $QS_2$ ($p$ = 0.016); TP vs. $QS_2$ ($p$ = 0.049) and HFnu vs. $QS_2$ ($p$ = 0.022)] respectively.

**Table 10.** Pearson's correlation between baseline STI and HRV parameters in IHD patients without MACE (n=185)

| | **PEP (ms)** | **LVET (ms)** | **$QS_2$ (ms)** | **PEP/LVET** |
|---|---|---|---|---|
| **Time-Domain parameters:** | | | | |
| **SDNN (ms)** | $r$ = 0.156<br>**$p$ = 0.034*** | $r$ = 0.109<br>$p$ = 0.139$^{NS}$ | $r$ = 0.190<br>**$p$ = 0.010*** | $r$ = 0.071<br>$p$ = 0.339$^{NS}$ |
| **rMSSD (ms)** | $r$ = 0.169<br>**$p$ = 0.022*** | $r$ = 0.088<br>$p$ = 0.232$^{NS}$ | $r$ = 0.177<br>**$p$ = 0.016*** | $r$ = 0.087<br>$p$ = 0.240$^{NS}$ |
| **Frequency-domain parameters:** | | | | |
| **TP ($ms^2$)** | $r$ = 0.143<br>$p$ = 0.051$^{NS}$ | $r$ = 0.069<br>$p$ = 0.353$^{NS}$ | $r$ = 0.145<br>**$p$ = 0.049*** | $r$ = 0.079<br>$p$ = 0.286$^{NS}$ |
| **LF ($ms^2$)** | $r$ = 0.027<br>$p$ = 0.719$^{NS}$ | $r$ = 0.064<br>$p$ = 0.388$^{NS}$ | $r$ = 0.075<br>$p$ = 0.312$^{NS}$ | $r$ = - 0.018<br>$p$ = 0.810$^{NS}$ |
| **HF ($ms^2$)** | $r$ = 0.148<br>**$p$ = 0.044*** | $r$ = 0.044<br>$p$ = 0.348$^{NS}$ | $r$ = 0.125<br>$p$ = 0.090$^{NS}$ | $r$ = 0.098<br>$p$ = 0.186$^{NS}$ |
| **Lfnu** | $r$ = - 0.138<br>$p$ = 0.060$^{NS}$ | $r$ = - 0.068<br>$p$ = 0.354$^{NS}$ | $r$ = - 0.142<br>$p$ = 0.054$^{NS}$ | $r$ = - 0.076<br>$p$ = 0.302$^{NS}$ |
| **HFnu** | $r$ = 0.042<br>$p$ = 0.567$^{NS}$ | $r$ = 0.155<br>**$p$ = 0.035*** | $r$ = 0.169<br>**$p$ = 0.022*** | $r$ = - 0.037<br>$p$ = 0.620$^{NS}$ |
| **LF/HF ratio** | $r$ = - 0.046<br>$p$ = 0.534$^{NS}$ | $r$ = -0.110<br>$p$ = 0.138$^{NS}$ | $r$ = 0.128<br>$p$ = 0.082$^{NS}$ | $r$ = 0.021<br>$p$ = 0.772$^{NS}$ |

**Moderately significant p ≤0.05; NS: Not significant*

***OBJECTIVE 4. To estimate the association of risk factors with STI and HRV among IHD patients.***

Pearson's correlations were accomplished to inspect the probable correlation between BMI and baseline STI and HRV. On correlation analysis $QS_2$ was negatively correlated with the BMI ($r$ = -0.157, $p$ = 0.028) denoting decrease in total electromechanical systole with the upsurge in BMI. (**Table 11**).

**Table 11.** Pearson's correlations between body mass index and systolic time intervals. (n=197)

| | **PEP (ms)** | **LVET (ms)** | **$QS_2$ (ms)** | **PEP/LVET** |
|---|---|---|---|---|
| **Body mass index (Kg/m$^2$)** | $r$ = - 0.073<br>$p$ = 0.305$^{NS}$ | $r$ = - 0.125<br>$p$ = 0.079$^{NS}$ | $r$ = - 0.156<br>**$p$ = 0.028$^{*}$** | $r$ = 0.006<br>$p$ = 0.928$^{NS}$ |

**Moderately Significant p ≤0.05; NS: Not significant.*

Furthermore, BMI had a significant negative correlation with the total power ($r$ = -0.161; $p$ = 0.024) and low frequency power ($r$ = -0.179; $p$ = 0.012), and high frequency power ($r$ = -0.189; $p$ = 0.008) HRV indices (**Table 12**) suggesting reduced autonomic tone/loss of vagal tone of heart/increase of sympathetic activity with increase in BMI.

**Table 12.** Pearson's correlations between BMI (Kg/m$^2$) and HRV parameters. (n=197)

| | **BMI (Kg/m$^2$)** |
|---|---|
| **Time-Domain parameters:** | |
| SDNN (ms) | $r$ = - 0.116<br>$p$ = 0.108$^{NS}$ |
| rMSSD (ms) | $r$ = - 0.107<br>$p$ = 0.138$^{NS}$ |

| | |
|---|---|
| **Frequency-domain parameters:** | |
| TP ($ms^2$) | *r* = - 0.161<br>***p* = 0.026*** |
| LF ($ms^2$) | *r* = - 0.179<br>***p* = 0.012*** |
| HF ($ms^2$) | *r* = - 0.189<br>***p* = 0.008*** |
| LFnu | *r* = 0.022<br>*p* = 0.760$^{NS}$ |
| HFnu | *r* = - 0.109<br>*p* = 0.127$^{NS}$ |
| LF/HF ratio | *r* = 0.076<br>*p* = 0.286$^{NS}$ |
| Heart rate | *r* = 0.107<br>*p* = 0.135$^{NS}$ |

**Moderately Significant p ≤0.05; NS: Not significant; BMI=body mass index*

Further, on admission clinical presentation, frequency distributions of risk factors are presented in **Table 13, Table 14, and Table 15** respectively.

**Table 13:** On admission clinical presentation of IHD in patients with and without MACE.

| VARIABLES | MACE | | Total (n=197) | P value |
|---|---|---|---|---|
| | No (n=185) | Yes (n=12) | | |
| Angina | | | | |
| • Negative | 7(3.8%) | 1(8.3%) | 8(4.1%) | 1.000$^{NS}$ |
| • Positive | 178(96.2%) | 11(91.7%) | 189(95.9%) | |
| Pain Score | | | | |
| • No pain | 76(41.1%) | 1(8.3%) | 77(39.1%) | **0.042**$^{*}$ |
| • Mild | 101(54.6%) | 11(91.7%) | 11(5.6%) | |
| • Moderate | 8(4.3%) | 0(0%) | 8(4.1%) | |
| Dyspnea | | | | |
| • No | 165(89.2%) | 9(75%) | 174(88.3%) | 0.308$^{NS}$ |
| • Yes | 20(10.8%) | 3(25%) | 23(11.7%) | |

*Chi-Square/Fisher Exact Test; *Moderately significant p ≤0.05; NS: Not significant.*

**Table 14:** Frequency distribution of diabetes mellitus and hypertension in relation to Outcome (with MACE and without MACE)

| | MACE | | Total (n=197) | P value |
|---|---|---|---|---|
| | No (n=185) | Yes (n=12) | | |
| DM | | | | |
| • No | 123(66.5%) | 4(33.3%) | 127(64.5%) | **0.044**$^{*}$ |
| • Yes | 62(33.5%) | 8(66.7%) | 70(35.5%) | |
| HTN | | | | |
| • No | 118(63.8%) | 7(58.3%) | 125(63.5%) | 1.000$^{NS}$ |
| • Yes | 67(36.2%) | 5(41.7%) | 72(36.5%) | |

*Chi-Square/Fisher Exact Test; *Moderately significant p ≤0.05; NS: Not significant; DM: Diabetes mellitus; HTN: Hypertension.*

**Table 15:** Frequency distribution of smoking/alcohol consumption/tobacco chewing in relation to Outcome (with MACE and without MACE)

| Variables | MACE | | Total (n=197) | P value |
|---|---|---|---|---|
| | No (n=185) | Yes (n=12) | | |
| Smoking | | | | |
| • No | 123(66.5%) | 9(75%) | 132(67%) | $0.777^{NS}$ |
| • Yes | 62(33.5%) | 3(25%) | 65(33%) | |
| Tobacco Chewing | | | | |
| • No | 177(95.7%) | 12(100%) | 189(95.9%) | $1.000^{NS}$ |
| • Yes | 8(4.3%) | 0(0%) | 8(4.1%) | |
| Alcohol Consumption | | | | |
| • No | 149(80.5%) | 10(83.3%) | 159(80.7%) | $0.888^{NS}$ |
| • Yes | 36(19.5%) | 2(16.7%) | 38(19.3%) | |

*Chi-Square/Fisher Exact Test; *Moderately significant p ≤0.05; + suggestive significance (P value: 0.05<p<0.10); NS: Not significant.*

**Multivariate tests** were performed to know the possible role of angina [(based on admission pain score of No pain/mild pain/moderate pain: 0-10)], smoking, tobacco chewing, alcohol consumption, and killip class on HRV and STIs. Results showed a significant association of angina with the HRV parameters ($p$ = 0.012). Besides, with the corrected model angina had a statistically significant effect on LFnu HRV parameter ($p$ = 0.031). Further, results showed no significant association of angina with the STIs. Predictors like smoking, tobacco chewing, alcohol consumption, and killip class had no significant association with the HRV indices. Whereas, with the corrected model, killip class had a statistically significant effect on total power HRV parameter ($p$ = 0.029). Furthermore, stated predictors had no significant association with the STIs. While, with the corrected model, tobacco chewing had a suggestive significant effect on LVET ($p$ = 0.069). Likewise, with the corrected model, killip class had a suggestive significant effect on PEP/LVET ($p$ = 0.055).

Multivariate tests were done to know whether diabetes mellitus (DM) and hypertension (HTN) has got any effect on HRV and STIs. Both DM and HTN had no significant association with any of the HRV and STIs. However, with the corrected model, hypertension had a suggestive significant effect on $QS_2$ ($p = 0.060$).

***OBJECTIVE 5.1. To evaluate the quality of life in post-PCI IHD patients with and without MACE.***

An independent t-test was performed to compare the post-PCI QoL measures in patients with and without MACE. A statistically significant difference between 3- and 6-month post-PCI PCS-12 scores were found between patients who had MACE and without MACE.

A two-way repeated measures ANOVA was performed to know the effect of PCI on quality of life among IHD patients (**Table 16)**. A significant variation amid pre- and post-PCI PCS-12 scores ($p = 0.039$) were found.

**Table 16.** Comparison of post-PCI QoL measures between IHD patients with and without MACE using independent t-test. QoL at 1-, 3-, and 6-month post-PCI using two-way repeated measures ANOVA

| QoL measures | MACE | | Total | *P* value | 2X3 Repeated ANOVA |
|---|---|---|---|---|---|
| | No | Yes | | | |
| PCS-12 | | | | | |
| • 1-month post-PCI | 51.15±6.26 | 46.69±1.94 | 51.04±6.22 | $0.221^{NS}$ | Group F=6.978, ***P*=0.009**$^{**}$; Time F=3.986, ***p*=0.039**$^{*}$ |
| • 3-month post-PCI | 52.86±2.56 | 48.67±4.62 | 52.75±2.68 | **0.007**$^{**}$ | |
| • 6-month post-PCI | 52.89±2.42 | 49.67±4.04 | 52.80±2.50 | **0.027**$^{*}$ | |
| MCS-12 | | | | | |
| • 1-month | 52.06±11.11 | 54.42±2.40 | 52.12±10.98 | $0.714^{NS}$ | Group |

| QoL measures | MACE | | Total | *P* value | 2X3 Repeated ANOVA |
|---|---|---|---|---|---|
| | No | Yes | | | |
| post-PCI | | | | | F=0.011, $P$=0.981$^{NS}$; Time F=0.020, $p$=0.887$^{NS}$ |
| • 3-month post-PCI | 53.96±5.19 | 54.00±1.73 | 53.96±5.12 | 0.988$^{NS}$ | |
| • 6-month post-PCI | 53.85±5.19 | 54.33±1.53 | 53.86±5.12 | 0.873$^{NS}$ | |

** Moderately significant (P value: 0.01< p ≤ 0.05); ** Strongly significant p ≤0.01; NS: Not significant*

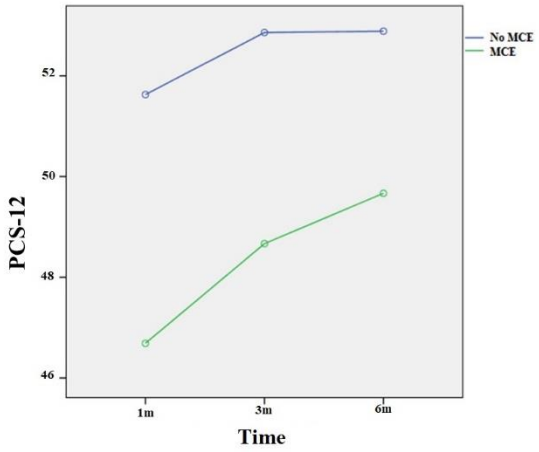



***Fig 13.*** *Physical component score (PCS-12) of quality of life at 1-, 3-, and 6-month post-PCI.*

Bonferroni post-hoc test for multiple comparisons found that the mean value of PCS-12 scores measured were significantly different between [1 month post-PCI] and [3 month post-PC] [$p$ = 0.000, 95% C.I. = -1.924 to -0.603]; [1 month post-PCI] and [6 month post-PCI] [$p$ = 0.000, 95% C.I. = -2.029 to -0.598]; [3 month post-PCI] and [1 month post-PCI] [$p$ = 0.000, 95% C.I. = 0.603 to 1.924] and [6 month post-PCI] and [1 month post-PCI] [$p$ = 0.000, 95% C.I. = 0.598, to 2.029] . There were no statistically significant differences between [3 month post-PCI] and [6 month post-PCI] ($p$=1.000) and [6 month post-PCI] and [3 month post-PCI] ($p$=1.000) PCS-12 scores.

**Table.** Pairwise Comparisons from Bonferroni post hoc test between 1-, 3-, and 6-month post-PCI PCS-12 scores.

| Time (I) | Time (J) | Mean Difference (I-J) | Std. Error | Sig.[b] | 95% Confidence Interval for Difference[b] | |
|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound |
| 1 | 2 | -1.264* | 0.272 | **0.000**** | -1.924 | -0.603 |
| | 3 | -1.313* | 0.295 | **0.000**** | -2.029 | -0.598 |
| 2 | 1 | 1.264* | 0.272 | **0.000**** | 0.603 | 1.924 |
| | 3 | -0.050 | 0.109 | 1.000NS | -0.314 | 0.214 |
| 3 | 1 | 1.313* | 0.295 | **0.000**** | 0.598 | 2.029 |
| | 2 | 0.050 | 0.109 | 1.000NS | -0.214 | 0.314 |

*Based on estimated marginal means *. the mean difference is significant at the 0.05 level. b. Adjustment for multiple comparisons: Bonferroni. NS: Not significant.*

***OBJECTIVE 5.2. To determine the association of quality of life in post-PCI IHD patients with STI and HRV.***

Pearson's correlation analysis was executed to distinguish the probable correlation between the quality of life and systolic time intervals. All Physical component (PCS-12) scores had no significant correlations with the STIs. Whereas, significant negative correlations were observed between Mental component/MCS-12 (3 month) scores and PEP (3 months) ($p$ = 0.020), MCS-12 (6 months) and PEP (6 months) ($p$ = 0.030), MCS-12 (1 month) and PEP/LVET (1 month) ($p$ = 0.043), MCS-12 (3 months) and PEP/LVET (3 months) ($p$ = 0.011), and MCS-12 (6 months) and PEP/LVET (6 months) ($p$ = 0.005) (**Table 17)**. Findings suggest low QoL in mental domain contributes to increased systolic time interval.

**Table 17.** Pearson's correlation between systolic time intervals and quality of life in IHD patients (n=121)

| | PCS-12 (1 month) | PCS-12 (3 months) | PCS-12 (6 months) | MCS-12 (1 month) | MCS-12 (3 months) | MCS-12 (6 months) |
|---|---|---|---|---|---|---|
| **PEP (ms) (1 month)** | *r* = 0.022<br>*p* = 0.808 | | | *r* = -0.108<br>*p* = 0.237 | | |
| **PEP (ms) (3 months)** | | *r* = -0.152<br>*p* = 0.096 | | | *r* = -0.211<br>***p* = 0.020*** | |
| **PEP (ms) (6 months)** | | | *r* = -0.007<br>*p* = 0.943 | | | *r* = -0.197<br>***p* = 0.030*** |
| **LVET (ms) (1 month)** | *r* = - 0.081<br>*p* = 0.379 | | | *r* = 0.140<br>*p* = 0.125 | | |
| **LVET (ms) (3 months)** | | *r* = - 0.104<br>*p* = 0.257 | | | *r* = 0.073<br>*p* = 0.429 | |
| **LVET (ms) (6 months)** | | | *r* = 0.027<br>*p* = 0.768 | | | *r* = 0.177<br>*p* = 0.052 |
| **$QS_2$ (ms) (1 month)** | *r* = - 0.065<br>*p* = 0.478 | | | *r* = 0.071<br>*p* = 0.437 | | |
| **$QS_2$ (ms) (3 months)** | | *r* = - 0.158<br>*p* = 0.084 | | | *r* = -0.025<br>*p* = 0.785 | |
| **$QS_2$ (ms) (6 months)** | | | *r* = 0.022<br>*p* = 0.807 | | | *r* = 0.084<br>*p* = 0.360 |
| **PEP/LVET (1 month)** | *r* = 0.050<br>*p* = 0.582 | | | *r* = -0.184<br>*p* = 0.043* | | |
| **PEP/LVET (3 months)** | | *r* = - 0.034<br>*p* = 0.711 | | | *r* = -0.231<br>***p* = 0.011*** | |
| **PEP/LVET (6 months)** | | | *r* = 0.003<br>*p* = 0.973 | | | *r* = -0.254<br>***p* = 0.005*** |

**Moderately significant p <0.05; NS: Not significant; PEP: Pre-ejection period; LVET: left ventricular ejection time; PCS-12: physical component score; MCS-12: Mental component score*

Pearson's correlation analysis was accomplished to recognize the possible correlation between the quality of life and HRV indices. All QoL parameters had no significant correlations with the HRV indices except the correlation between Physical component/PCS-12 (1 month) scores and SDNN (1 month) with $p = 0.026$ (**Table 18)**. Findings indicate low QoL in the physical domain contributes to increased heart rate variability.

**Table 18.** Pearson's correlation between HRV and quality of life in IHD patients (n=121)

| | **PCS-12 (1 month)** | **PCS-12 (3 months)** | **PCS-12 (6 months)** |
|---|---|---|---|
| **Time-Domain parameters:** | | | |
| SDNN (ms) (1 month) | $r = -0.203$<br>$\mathbf{p = 0.026^{*}}$ | | |
| SDNN (ms) (3 months) | | $r = 0.007$<br>$p = 0.937^{NS}$ | |
| SDNN (ms) (6 months) | | | $r = 0.028$<br>$p = 0.761^{NS}$ |
| rMSSD (ms) (1 month) | $r = -0.167$<br>$p = 0.06^{NS}$ | | |
| rMSSD (ms) (3 months) | | $r = 0.010$<br>$p = 0.916^{NS}$ | |
| rMSSD (ms) (6 months) | | | $r = -0.011$<br>$p = 0.907^{NS}$ |
| **Frequency-domain parameters:** | | | |
| TP ($ms^2$) (1 month) | $r = -0.148$<br>$p = 0.106^{NS}$ | | |
| TP ($ms^2$) (3 months) | | $r = 0.043$<br>$p = 0.641^{NS}$ | |
| TP ($ms^2$) (6 months) | | | $r = 0.075$<br>$p = 0.413^{NS}$ |

| | PCS-12 (1 month) | PCS-12 (3 months) | PCS-12 (6 months) |
|---|---|---|---|
| LF ($ms^2$) (1 month) | $r$ = -0.055<br>$p$ = 0.549$^{NS}$ | | |
| LF ($ms^2$) (3 months) | | $r$ = -0.001<br>$p$ = 0.988$^{NS}$ | |
| LF ($ms^2$) (6 months) | | | $r$ = 0.108<br>$p$ = 0.237$^{NS}$ |
| HF ($ms^2$) (1 month) | $r$ = -0.167<br>$p$ = 0.493$^{NS}$ | | |
| HF ($ms^2$) (1 month) | | $r$ = 0.028<br>$p$ = 0.762$^{NS}$ | |
| HF ($ms^2$) (1 month) | | | $r$ = 0.045<br>$p$ = 0.626$^{NS}$ |
| LFnu (1 month) | $r$ = 0.022<br>$p$ = 0.808$^{NS}$ | | |
| LFnu (3 months) | | $r$ = 0.010<br>$p$ = 0.912$^{NS}$ | |
| LFnu (6 months) | | | $r$ = 0.028<br>$p$ = 0.764$^{NS}$ |
| HFnu (1 month) | $r$ = 0.022<br>$p$ = 0.811$^{NS}$ | | |
| HFnu (3 months) | | $r$ = 0.035<br>$p$ = 0.702$^{NS}$ | |
| HFnu (6 months) | | | $r$ = - 0.015<br>$p$ = 0.874$^{NS}$ |
| LF/HF ratio (1 month) | $r$ = -0.055<br>$p$ = 0.549$^{NS}$ | | |
| LF/HF ratio (3 months) | | $r$ = -0.016<br>$p$ = 0.862$^{NS}$ | |
| LF/HF ratio (6 months) | | | $r$ = - 0.035<br>$p$ = 0.700$^{NS}$ |

**Moderately significant p ≤0.05; NS: Not significant; PCS-12: physical component score.*

***OBJECTIVE 6. To study the ability of 24h post-PCI STI and HRV indices in predicting the occurrence of MACE among IHD patients***

Sensitivity, Specificity, area under the curve and cut-off values with 95% confidence intervals of all 24h post-PCI STI and HRV were found. None of the STIs presented the best discriminatory power (area under the ROC curve ≥0.650) for the occurrence of Major adverse cardiac events **(Table 19).**

**Table 19.** Sensitivity, Specificity, and area under the ROC curve of the 24h post-PCI STI values to assess the presence of Major adverse cardiac events (n=145).

| **Pre-discharge STI values** | **Sensitivity** | **Specificity** | **Cut-off values** | **AUC** | **95 % CI** | ***p*-value** |
|---|---|---|---|---|---|---|
| PEP (ms) | 57% | 53% | 85.50 | 0.601 | 0.371-0.832 | $0.366^{NS}$ |
| LVET (ms) | 86% | 53% | 288.50 | 0.606 | 0.461-0.750 | $0.347^{NS}$ |
| $QS_2$ (ms) | 71% | 51% | 372.50 | 0.677 | 0.504-0.849 | $0.116^{NS}$ |
| PEP/LVET | 57% | 51% | 0.292 | 0.555 | 0.327-0.784 | $0.622^{NS}$ |

*AUC: area under the curve; CI: confidence interval; Normalized STI values: Cut-off Values; * Moderately significant p ≤0.05; NS: Not significant.*

Whereas, total power (AUC=0.734; *p*=0.037) and LF (AUC=0.733; *p*=0.038) HRV indices showed greater prognostic accuracy for the occurrence of MACE. (**Table 20 and Fig. 14a and 14b)**

**Table 20.** Sensitivity, Specificity, and area under the ROC curve of the 24h post-PCI HRV values to assess the presence of Major adverse cardiac events (n=145).

| **Pre-discharge HRV indices** | **Sensitivity** | **Specificity** | **Cut-off values** | **AUC** | **95 % CI** | ***p*-value** |
|---|---|---|---|---|---|---|
| **SDNN (ms)** | 57% | 67% | 44.49 | 0.694 | 0.521-0.866 | $0.085^{NS}$ |
| **rMSSD (ms)** | 71% | 63% | 36.4 | 0.668 | 0.433-0.902 | $0.135^{NS}$ |
| **TP ($ms^2$)** | 86% | 61% | 1225.73 | 0.734 | 0.592-0.876 | **0.037*** |
| **LF ($ms^2$)** | 71% | 69% | 267.93 | 0.733 | 0.555-0.911 | **0.038*** |

| | | | | | | |
|---|---|---|---|---|---|---|
| **HF ($ms^2$)** | 71% | 73% | 417.9 | 0.689 | 0.464-0.915 | $0.091^{NS}$ |
| **LF/HF ratio** | 43% | 70% | 0.52 | 0.427 | 0.160-0.693 | $0.513^{NS}$ |

*AUC: area under the curve; CI: confidence interval; Normalized HRV values: Cut-off Values; * Moderately significant p ≤0.05.*

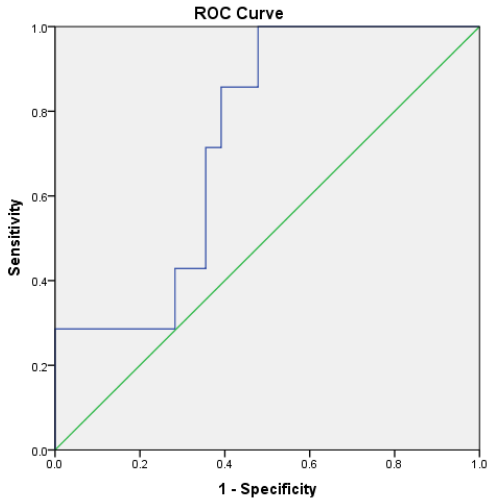



***Fig 14a.*** *Sensitivity and Specificity of the total power HRV index to assess the presence of MACE.*

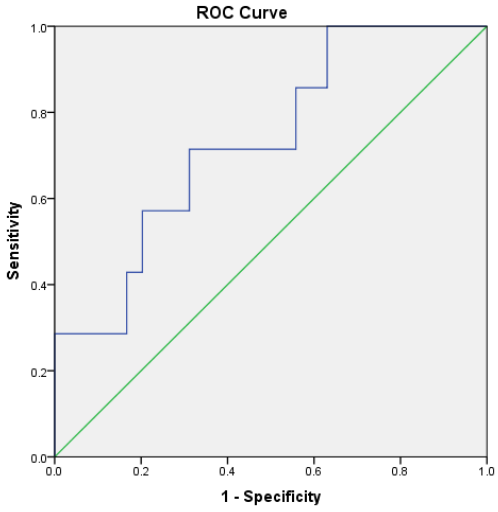



***Fig 14b.*** *Sensitivity and Specificity of the low frequency power HRV index to assess the presence of MACE.*

# *DISCUSSION*

# DISCUSSION

On admission, among IHD patient's PEP and PEP/LVET ratios were higher when compared to 24h post-PCI. Whereas, LVET increased in 24h post-PCI and sustained 6 months post-PCI as compared to baseline values recorded on admission. While the duration of total electro-mechanical systole (PEP and LVET) was increased at 24h post-PCI and decreased thereafter in 3 months this did not reach baseline even after 6 months. Findings suggest that there was a gradual reversal of sympathetic dominance and restoration of parasympathetic tone.

Furthermore, admission SDNN, rMSSD, TP, LF, HF, and HFnu HRV values were higher when compared to 24h post-PCI with the LFnu and LF/HF ratios being lesser. Besides, when compared to 24h post-PCI HRV values, there was an increase in SDNN, rMSSD, LF, HF, and HFnu with a decrease in LFnu and LF/HF ratios at 3- and 6-month post-PCI which did not reach baseline even after 6-months. Hence, it was shown that successful revascularization would cause only a partial stabilization of vagal tone among IHD patients.

Also, the average heart rate raised 24h post-PCI which was consistent with enhanced sympathetic activity and a decrease in parasympathetic activity. Later, it was observed that there was a significant reduction in heart rate over time. Hence, findings suggested a decrease in sympathetic activity in patients with IHD following revascularization was gradual at 3 months post-PCI when compared to 24h post-PCI. These outcomes could be explained by the amplified state of sympathetic hyperactivity provoked due to acute stress or anxiety of surgical procedure, which might have prevented HRV increase immediately after successful revascularization. It was observed that the increase of SDNN post-PCI was significant in subjects without pre-procedural anxiety compared with those with anxiety. (**Delewi *et al.* 2016**) In the present study, during pre-PCI ECG recordings angina/anxiety persisted in a few patients. On multivariate analysis, it was revealed that angina had a significant association

with the HRV parameters ($p$=0.012) especially LFnu ($p$=0.031) HRV index on admission. While a significant association of angina was observed with the PEP ($p$=0.002) and PEP/LVET ratios ($p$=0.001) also.

Also, it was observed in our study that there was a significant prolongation in PEP and PEP/LVET ratios on admission in patients who had MACE. Whereas, as time progressed we observed that there was an overall increase in LV performance as indicated by a significant decrease in PEP and PEP/LVET post-PCI over time. All these findings suggested enhanced pumping ability of the left ventricle in patients with IHD following revascularization gradually yet significantly. **Reant P *et al.* 2010** showed with the increase in LV ejection fraction, PEP was significantly prolonged, and LVET significantly decreased, resulting in a significantly prolonged PEP/LVET ratio in 134 patients with heart failure. In addition, in the current study, there was a significant increase in SDNN, rMSSD, HF, and TP short-term linear HRV indices on admission in patients who had MACE.

To the best of our knowledge, this is the novel attempt to execute the simultaneous monitoring of STI and HRV. On admission, STIs exhibited a significant positive correlation with the HRV indices. Based on the literature, [46] findings suggested that simultaneous monitoring of STI and HRV could be an ideal tool to assess cardiac autonomic function among IHD patients. Accordingly, STIs may offer valuable understanding regarding cardiac sympathetic (LVET) activity to complement the cardiac parasympathetic (HF) activity of HRV among IHD patients. On the contrary, **Sharma R *et al.* 2001** observed no significant correlation between different STIs and autonomic functions. Hence results indicated autonomic functions and STI could be independent predictors of normal cardiovascular functioning.

In our study, we found a significant negative correlation between the quality of life (MCS-12) and PEP, PEP/LVET ratios. Furthermore, the correlation between the quality of life (PCS-12) and SDNN was witnessed. Findings suggest low QoL in the mental domain (MCS-12) contributes to increased STI (PEP and PEP/LVET ratios), while low QoL in the physical domain (PCS-12) contributes to increased HRV (SDNN). The present study results were in line with a study by **Lu Wan-Chun *et al.* 2016** where 329 mentally and physically healthy adults completed the Beck Anxiety questionnaire on quality of life. The findings of this study pointed to a presumed underlying mechanism by which low $HRQOL_{physical}$ conferred elevated risks for CVD and demonstrated the independent function of low $HRQOL_{physical}$ in reducing HRV in healthy persons.

Besides, on correlation analysis $QS_2$ correlated negatively with the body mass index (BMI) denoting decrease in the duration of total electro-mechanical systole with the upsurge in BMI in the current study. Previous literature had recruited 98 healthy MBBS students (19 to 21 years) wherein peripheral arterial pressures and cardiac intervals (PEP, ejection time, Upstroke time, Deceleration time, pulse duration, and ejection slope) were determined by PeriScope™. Consequently, the authors suggested when drawing conclusions on LV performance, gender, anthropometric measurements, and blood pressure should be considered because they have an impact on cardiac time intervals. (**Sadaf *et al.* 2020**)

In addition, BMI had a significant negative correlation with the TP, LF, and HF HRV indices suggesting reduced autonomic tone with an increase in BMI. Findings are on par with the literature which says increased BMI can independently decrease HRV, particularly when central adiposity is present.[65] Our study which had comprised of 197 IHD patients, among them 50% belonged to the overweight (BMI: 25-29.9 $kg/m^2$; 41.1%) to obese category (BMI: ≥30 $kg/m^2$; 17%). **Windham *et al.* 2012** analyzed time domain HRV variables (SDNN and rMSSD) from 24-hour Holter monitoring in 159 participants (29 to 96 years). The authors

observed that an increase in waist circumference was associated with a decrease in SDNN and rMSSD in younger individuals. Accordingly, central adiposity possibly will contribute to sympathetic and parasympathetic autonomic nervous system failures early in life. **Yadav *et al.* 2017** recruited 29 healthy controls of normal weight (BMI 18–24 kg/$m^2$) and 30 adult obese subjects (BMI >30 kg/$m^2$). Waist-hip ratio (WHR) significantly correlated positively with LFnu (r = 0.478, $p$ <0.01) and LF/HF ratio ($r$ = 0.479, $p$ <0.01) according to Spearman's correlation between HRV and obesity indices, whereas HF ($r$ = 0.374, $p$ <0.05) and HFnu ($r$ = 0.478, $p$ <0.01) significantly correlated negatively with WHR. Hence, increased WHR would be strongly associated with reduced cardiac parasympathetic and increased sympathetic activity in obese individuals defined by BMI.

The present study results revealed that smoking, tobacco chewing, alcohol consumption, and Killip class had no significant association with any of the HRV measures or the systolic time intervals. Whereas with the corrected model, the Killip class had a significant ($p$ = 0.029) effect on the total power HRV index and which might have had a possible role to play in cardiac autonomic dysfunction. Whereas according to a meta-analysis, when compared to persons who smoke 20 cigarettes per day, people who smoke only around one cigarette per day have a substantially higher than expected risk of getting coronary heart disease and stroke.[29] According to a systematic review and meta-analysis by **Roerecke and Rehm 2014** there is no dependable proof that persistent excessive drinking and IHD are protective of one another. Therefore, excessive drinking of any kind should be avoided.

The present study results revealed that both DM and HTN had no significant association with any of the HRV measures or the STIs. While **Bassi *et al.* 2018** found that patients with T2DM and HTN exhibited lower values of mean R-R intervals when compared with patients who had only T2DM. Accordingly, HTN has got a negative influence on the cardiac autonomic function in diabetes mellitus. However, a review by **Benichou *et al.* 2018** included

25 case-control studies; which consisted of 1,356 patients with T2DM and 1,576 healthy controls. T2DM patients had significantly lower R-R intervals, lower SDNN, lower rMSSD, lower pNN50, lower TP, lower LF, and lower HF.

A study by **Wennerbloom B *et al.* 1998** enrolled thirty-two patients (32 to 81 years) with recently developed angina, Holter-monitored 24–48h at baseline and after 4 to 5 days. Patients were on isosorbide-5-mononitrate (IS-5-MN), metoprolol, and the combined treatment. Wherein, IS-5-MN had no effect on HRV. While, the current study patients were on (n=187/197) nicorandil, isosorbide dinitrate, nitroglycerin, ranolazine, ivabradine, isosorbide mononitrate, carvedilol antianginal drugs. Where the antianginal drugs ($p$ = 0.004) and antiarrhythmics ($p$ = 0.023) had a significant effect on LVET ($p$ = 0.006) and $QS_2$ ($p$ = 0.019). Whereas, in a study by **Perrot *et al*. 1997** using programmed ventricular stimulation, 50 individuals with cardiac illness and spontaneous sustained ventricular tachycardia (VT) were investigated for HRV. They observed the outcome of treatment is not predicted by the initial HRV. Despite the antiarrhythmics' ability to prevent VT, quinidines and amiodarone tend to lower HRV. Present study patients were on (n=04/197) amiodarone and digoxin antiarrhythmics in whom a significant effect of antiarrhythmics on LVET ($p$ = 0.006) and $QS_2$ ($p$ = 0.019) were observed.

In the current study, a statistically significant difference between 3- and 6-month post-PCI PCS-12 scores was found between ACS patients who had MACE and without MACE. Besides, it was observed that there was a significant increase in the physical component score of QoL with a non-significant increase in the mental component score of QoL post-PCI over time when compared to 1-month post-PCI QoL scores. Furthermore, almost all QoL parameters had significant correlations with the LVEF. Results indicated QoL measurement after PCI could be a valuable tool to study the health-related QoL among ACS survivors.

**Anchah *et al*. 2017** enrolled 112 patients with newly identified ACS. Based on Malaysian norms, at baseline, 6 months, and 12 months post-discharge authors compared the pre- and post-quality of life of three groups (intervention [modified Cardiac Rehabilitation Programme (MCRP)], conventional, and control), respectively. Short-Form 36 Questionnaire was used to procure QoL data. At the end of the 12-month follow-up, the MCRP participants accomplished well in their PCS than those in the conventional CRP and control groups.

Also, in this study, we show that, in ACS patients treated by PCI, HRV assessed 24h post-PCI using Lead-II ECG was the independent predictor of MACE, including death and re-AMI. Sensitivity and specificity values of 24h post-PCI HRV indices were also evaluated.

As a main finding, we found that the indices which presented the best discriminatory power for the occurrence of MACE were TP $\leq$1225.73 $ms^2$ and LF $\leq$267.93 $ms^2$. While a study by **Balanescu S *et al.* 2004** assessed the prognostic value of HRV parameters 1 year after AMI treated conventionally or by a reperfusion method in the first 12 hours from the symptom onset. The authors had included 463 consecutive patients with AMI 60.6±13.0 years old. Two hundred and eleven patients were treated by thrombolysis or primary percutaneous transluminal coronary angioplasty; the other 251 patients received conventional therapy. Results of the study showed the incidence of cardiac death was 14.7%, while that of sudden death was 4.8%. Both were higher in patients treated conventionally. Patients treated by reperfusion had higher HRV parameters reflecting both vagal and sympathetic activity (SDNN and total power) as well as those expressing only vagal output (rMSSD and HF power) than conventionally treated subjects. The variables independently correlated with 1-year survival were SDNN <50 ms, rMSSD <20 ms, LF/HF >2, non-sustained ventricular tachycardia, and LVEF <40%.

Also, **Coviello *et al.* 2013** measured the prognostic value of HRV in STEMI patients treated by PTCA and optimal medical therapy among 182 patients with a first STEMI (59.1±8.11 years). At a follow-up of 42±23 months, MACE occurred in 14 patients (7.6%; 3 deaths and 11 re-AMIs). They observed HRV parameters before discharge were significantly lower in patients with MACE, with SDNN, very LF, and LF amplitude being the most predictive variables.

# *SUMMARY AND*

# *CONCLUSION*

## *SUMMARY AND CONCLUSION*

In conclusion, the study showed on admission PEP and PEP/LVET ratios were higher when compared to 24h post-PCI in IHD patients. Whereas, LVET increased in 24h post-PCI and sustained 6 months post-PCI as compared to on admission values. While the duration of total electro-mechanical systole (PEP and LVET) was increased at 24h post-PCI and decreased thereafter in 3 months.

Likewise, admission SDNN, rMSSD, TP, LF, HF, and HFnu HRV values were higher when compared to 24h post-PCI with the LFnu and LF/HF ratios being lesser. Further, when compared to 24h post-PCI HRV values, there was an increase in SDNN, rMSSD, LF, HF, and HFnu with a decrease in LFnu and LF/HF ratios at 3- and 6-month post-PCI.

Follow-up analysis showed a significant rise in HRV and a reduction in STIs indicating gradual but significant restoration in cardiac autonomic tone.

Similarly, it was observed that there was a significant prolongation in PEP and PEP/LVET ratios at baseline in patients who had MACE. As time progressed there was a significant decrease in PEP and PEP/LVET ratios when compared to 24h post-PCI STI values.

Also, a significant increase in baseline SDNN, rMSSD, HF, and TP was seen in patients who had MACE. The resultant sensitivity and specificity of HRV are still limited in the present study. Particularly, its sensitivity is higher (43% to 86%) with a modest specificity (61% to 73%). Moreover, when compared to 24h post-PCI HRV values there was an overall increase in SDNN, rMSSD, HF, LFnu, and HFnu with a significant decrease in LF/HF ratio 3- and 6-month post-PCI. A decrease in 24h post-PCI HRV values implied that this surgical treatment might have altered the cardiac autonomic balance.

Further, 1-month post-PCI QoL PCS-12 scores were higher in IHD patients without MACE when compared to the patients who had MACE. Besides, their MCS-12 scores were lower in patients who escaped MACE when compared to patients with MACE. Still, PCS-12 scores increased significantly 3-and 6-month post-PCI with MCS-12 scores being no significant change when compared to 1-month post-PCI scores.

Heart rate variability being a non-invasive, inexpensive, and simple technique perhaps clinically be useful in the prognostic evaluation of the incidence of adverse events in patients with acute coronary syndrome.

Besides, with the help of pulsed-Doppler echocardiography, the current study could precisely assess STIs as a measure of LV systolic function in patients with IHD. In addition, close monitoring of STIs may help to recognize subjects with early LV dysfunction and also in the management of IHD. Assessment of STI would give us significant information about LV contractility and early indicator of the severity of LV systolic dysfunction.

# *STRENGTHS AND LIMITATIONS*

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## STRENGTHS OF THE STUDY

- Not many studies are available wherein the measurement of STI was done using the pulsed-Doppler technique.
- Likewise, the current study incorporated simultaneous monitoring of HRV and STI to evaluate the cardiac autonomic function, which is also a novel attempt.
- The study was conducted using an adequate sample size with 90% power. Hence the results of this study could be helpful to clinicians in the management of IHD and their QoL.
- Inter-observer bias was less likely because the study was conducted by a single researcher.

## LIMITATIONS OF THE STUDY

- Despite a long recruitment period, the present study was conducted in a single center only. The utility of HRV or STI as one of the prognostic evaluators for IHD must therefore be further validated by multi-centric large-scale randomized trials.
- Additionally, pre-procedural anxiety was not evaluated in the current investigation, which would have provided us with additional context for the post-PCI variation in HRV or STI indices.

# *BIBLIOGRAPHY*

# BIBLIOGRAPHY


1. "Coronary artery disease." *Wikipedia*. Last edited on 21/9/2022. https://en.m.wikipedia.org/wiki/Coronary_artery_disease.
2. "CPK-MB test." *Wikipedia*. Last edited on 22/4/2022. https://en.wikipedia.org /wiki/CPK-MB_test.
3. "Electrocardiography." *Wikipedia*. Last edited on 27/9/2022. https://en. wikipedia.org/ wiki/Electrocardiography.
4. "Myocardial infarction." *Wikipedia*. Last edited on 22/9/2022. https://en.wikipedia.org/ wiki/Myocardial_infarction.
5. "Toponin." *Wikipedia*. Last edited on 19/9/2022. https://en.wikipedia.org/wiki/Troponin_I.
6. "Transthoracic echocardiogram." *Wikipedia*. Last edited on 31/7/2022. https://en.wikipedia.org/wiki/Transthoracic_echocardiogram.
7. Abdul Qahar Sarwari. The relationship between interpersonal communication competence, intercultural communication competence and heart rate variability among international postgraduate students. Available from: https://www.researchgate. net/figure /Functions-of-the-heart-in-the-autonomic-nervous system_fig1_332187196 [accessed 3 Oct, 2022].
8. Abrootan S, Yazdankhah S, Payami B, Alasti M. Changes in Heart Rate Variability Parameters after Elective Percutaneous Coronary Intervention. J TehUniv Heart Ctr. April 3 2015;10(2):80-84. PMCID: PMC4477091. PMID: 26110006
9. Anchah L, Hassali MA, Lim MS, Ibrahim MI, Sim KH, Ong TK. Health related quality of life assessment in acute coronary syndrome patients: the effectiveness of early phase

I cardiac rehabilitation. Health Qual Life Outcomes. 2017 Jan 13;15(1):10. doi: 10.1186/s12955-016-0583-7. PMID: 28086784; PMCID: PMC5237194.

10. Azmi, Soraya & Goh, Adrian & Fong, Alan & Anchah, Lawrence. (2015). Quality of life among Patients with Acute Coronary Syndrome in Malaysia. Value in Health Regional Issues. 6. 80-83. 10.1016/j.vhri.2015.03.015.

11. Bahall M, Khan K. Quality of life of patients with first-time AMI: a descriptive study. Health Qual Life Outcomes. 2018 Feb 13;16(1):32. doi: 10.1186/s12955-018-0860-8. PMID: 29433517; PMCID: PMC5810028.

12. Balanescu S, Corlan AD, Dorobantu M, Gherasim L. Prognostic value of heart rate variability after acute myocardial infarction. Med Sci Monit. 2004 Jul;10(7):CR307-15. Epub 2004 Jun 29. PMID: 15232505.

13. Barrett KE, Ganong WF. Ganong's review of medical physiology. 23rd ed. McGraw-Hill Medical; McGraw-Hill [distributor], New York, London, ©2012.

14. Bassi D, Cabiddu R, G Renata. Mendes, Tossini N, M Vivian, et al. Effects of Coexistence Hypertension and Type II Diabetes on Heart Rate Variability and Cardiorespiratory Fitness. *Arq. Bras. Cardiol* 2018; 111(1): 64-72. DOI: 10.5935/abc.20180105

15. Benichou T, Pereira B, Mermillod M, Tauveron I, Pfabigan D, Maqdasy S, et al. (2018) Heart rate variability in type 2 diabetes mellitus: A systematic review and meta±analysis. *PLoS ONE* 13(4): e0195166. https://doi.org/10.1371/journal. pone.0195166.

16. Biering-Sørensen T, Querejeta Roca G, Hegde SM, Shah AM, Claggett B, Mosley TH Jr, Butler KR Jr, Solomon SD (2018) Left ventricular ejection time is an independent

predictor of incident heart failure in a community-based cohort. Eur J Heart Fail. 20(7):1106-1114. doi: 10.1002/ejhf.928.

17. Braunwald E. Unstable angina: a classification. Circulation.1989; 80:410–414. https://doi.org/10.1161/01.CIR.80.2.410.

18. Brembilla-Perrot B, Alsagheer S, Jacquemin L, Beurrier D, Retournay G, Grentzinger A. Influence des anti-arythmiques sur la variabilité de la fréquence cardiaque [Influence of anti-arrhythmia agents on heart rate variability]. Ann Cardiol Angeiol (Paris). 1997 Mar;46(3):129-34. French. PMID: 9183392.
19. Chen X, Xin Y, Hu W, Zhao Y, Zhang Z, Zhou Y (2019) Quality of life and outcomes in heart failure patients with ejection fractions in different ranges. PLoS ONE 14(6): e0218983. https://doi.org/10.1371/journal.pone.0218983.
20. Compostella L, Lakusic N, Compostella C, Truong LVS, Iliceto S, Bellotto F. Does heart rate variability correlate with long term prognosis in myocardial infarction patients treated by early revascularization? World J Cardiol 2017; 9(1): 27-38.

21. Coviello I, Pinnacchio G, Laurito M, Stazi A, Battipaglia I, Barone L, et al. Prognostic Role of Heart Rate Variability in Patients with ST-Segment Elevation Acute Myocardial Infarction Treated by Primary Angioplasty. Cardiology 2013; 124:63–70. DOI: 10.1159/000345779.

22. D Venkatesh, Shenoy AR, S Prakash V. Alteration of heart rate variability in patients with coronary artery disease. Natl J Physiol Pharm Pharmacol. 2018; 8(6):820-823. DOI: 10.5455/njppp.2018.8.0103230012018.
23. Delewi R, Rohling WJ,Wagenaar TC, Zwemstra M, Meesterman GM, Vis MM, et al. Anxiety levels of patients undergoing coronary procedures in the catheterization

laboratory, *International Journal of Cardiology* (2016). doi:10.1016/j.ijcard.2016.11.043.

24. Failde I, Medina P, Ramírez C, Arana R. Assessing health-related quality of life among coronary patients: SF-36 vs SF-12. Public Health. 2009 Sep;123(9):615-7. doi: 10.1016/j.puhe.2009.07.013. Epub 2009 Sep 2. PMID: 19729176.

25. Forslund L, Björkander I, Ericson M, Held C, Kahan T, Rehnqvist N, Hjemdahl P. Prognostic implications of autonomic function assessed by analyses of catecholamines and heart rate variability in stable angina pectoris. *Heart* 2002;87:415-422.

26. Georgoulias, Panagiotis & Angelidis, George & Zisimopoulos, Athanasios & Tsougos, Ioannis. (2016). Myocardial Perfusion (SPECT) Imaging: Radiotracers and Techniques. 10.2174/978168108377311602000 7.

27. Gomes ME, Aengevaeren WR, Lenders JW, Verheugt FW, Smits P, Tack CJ. Improving myocardial perfusion by percutaneous coronary intervention reduces central sympathetic activity in stable angina. Clin Cardiol 2009;33:E16-21.

28. González-Chica DA, Dal Grande E, Bowden J, Musker M, Hay P, Stocks N. Are we reducing the risk of cardiovascular disease and improving the quality of life through preventive health care? Results of a population-based study in South Australia. Prev Med. 2017 Jun;99:164-170. doi: 10.1016/j.ypmed.2017.02.007. Epub 2017 Feb 20. PMID: 28219783.

29. Hackshaw A, Morris JK, Boniface S, Tang JL, Milenković D. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. BMJ. 2018 November 28;363:k5035. PMCID: PMC5781309. PMID: 29367388. DOI: 10.1136%2Fbmj.j5855

30. Hall JE, Guyton AC. Guyton and Hall textbook of medical physiology. 11th ed. Saunders Elsevier, Philadelphia, PA, ©2011.
31. Harris PR, Stein PK, Fung GL, Drew BJ. Heart rate variability measured early in patients with evolving acute coronary syndrome and 1-year outcomes of rehospitalization and mortality. Vasc Health Risk Manag. 2014 Aug 5;10:451-64. doi: 10.2147/VHRM.S57524.s
32. Hassan S, Turner P. Systolic time intervals: a review of method in the non-invasive investigation of cardiac function in health, disease and clinical pharmacology. Postgraduate Medical Journal. July 1983;59:423-434.
33. Heart rate variability standards of measurement, physiological interpretation, and clinical use Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology (Membership of the Task Force listed in the Appendix) European Heart Journal. 1996;17:354–381.
34. Hijazi W, Jolly SS, Budaj A, Beręsewicz A, Undas A. Ischemic Heart Disease (IHD). McMaster Textbook of Internal Medicine. Kraków:Medycyna Praktyczna. Available from: https://empendium.com/mcmtextbook-sae/chapter/B78.II.2.5.?rfmcm. [Last accessed on 2022 Aug 02].
35. Huffman MD, Mohanan PP, Devarajan R, Baldridge AS, Kondal D, Zhao L, Ali M, Spertus JA, Chan PS, Natesan S, Abdullakutty J, Krishnan MN, Tp A, Renga S, Punnoose E, Unni G, Prabhakaran D, Lloyd-Jones DM; ACS QUIK Investigators. Health-Related Quality of Life at 30 Days Among Indian Patients With Acute Myocardial Infarction. Circ Cardiovasc Qual Outcomes. 2019 Feb;12(2):e004980. doi: 10.1161/CIRCOUTCOMES.118.004980.

36. Huikuri HV, Mäkikallio TH, Peng CK, Goldberger AL, Hintze U, Moller M, DIAMOND Study Group. Fractal correlation properties of R–R interval dynamics and mortality in patients with depressed left ventricular function after an acute myocardial infarction. Circulation 2000;101:47–53.

37. Killip 3rd T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. Am J Cardiol. 1967;20(4):457–464.

38. Korobka IE, Yakovleva EG, Belonosov SS, Zarubina TV, Korotkov KG. Gender differences in the activity of the autonomic nervous systems of healthy and hypertensive patients in Russia. J Appl Biotechnol Bioeng. 2017;3(6):459–463.

39. Kuzemczak M, Białek-Ławniczak P, Torzyn´ ska K, Janowska-Kulin´ ska A, Miechowicz I, Kramer L et al. Comparison of Baseline Heart Rate Variability in Stable Ischemic Heart Disease Patients with and without Stroke in Long-Term Observation. *Journal of Stroke and Cerebrovascular Diseases*. 2016 Oct; 25(10): pp 2526–2534.

40. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Impact of Physical Inactivity on the World's Major Non Communicable Disease. Lancet. July 21 2012;380(9838):219–229. doi:10.1016/S0140-6736(12)61031-9.

41. Lewis RP, Rittogers SE, Froester WF, Boudoulas H. A critical review of the systolic time intervals. Circulation. 1 Aug 1977; 56: 146–158.DOI: 10.1161/01.CIR.56.2.146.

42. Lu WC, Tzeng NS, Kao YC, Yeh CB, Kuo TB, Chang CC, Chang HA. Correlation between health-related quality of life in the physical domain and heart rate variability in asymptomatic adults. Health Qual Life Outcomes. 2016 Oct 21;14(1):149. doi: 10.1186/s12955-016-0555-y. PMID: 27765048; PMCID: PMC5073888.

43. Mäkikallio TH, Huikuri HV, Hintze U, et al, DIAMOND Study Group (Danish Investigations of Arrhythmia and Mortality ON Dofetilide). Fractal analysis and time and frequency-domain measures of heart rate variability as predictors of mortality in patients with heart failure. Am J Cardiol 2001;87:178–82.
44. Martini FH. Fundamentals of Anatomy and Physiology. 8th ed. 2006. Chapter20, by permission of Pearson Education, Inc Prentice Hall, copyright © 2006.864 Circulation August 19, 2008.
45. Melville MR, Lari MA, Brown N, Young T, Gray D. Quality of life assessment using the short form12 questionnaire is as reliable and sensitive as the short form 36 in distinguishing symptom severity in myocardial infarction survivors. *Heart* 2003;89:1445–1446.
46. Michael S, Graham KS and Davis GM OAM (2017) Cardiac Autonomic Responses during Exercise and Post-exercise Recovery Using Heart Rate Variability and Systolic Time Intervals—A Review. Front. Physiol. 8:301. doi: 10.3389/fphys.2017.00301.
47. Miyase Y, Miura S, Shiga Y, Nakamura A, Norimatsu K, Nishikawa H, Saku K. The ratio of low-frequency to high-frequency in ambulatory electrocardiographic monitoring immediately before coronary angiography as a predictor of the presence of coronary artery disease. *J Clin Med Res* 2014;6:36-43.
48. Pernaje Seetharam S, Shankar Ms V, Udupa K, A R, Reddy N. Prognostic value of heart rate variability in acute coronary syndrome. J Basic Clin Physiol Pharmacol. 2022 Oct 4. doi: 10.1515/jbcpp-2022-0134. Epub ahead of print. PMID: 36194293.
49. Pivatelli FC, Dos Santos MA, Fernandes GB, Gatti M, de Abreu LC, Valenti VE, Vanderlei LC, Ferreira C, Adami F, de Carvalho TD, Monteiro CB, de Godoy MF.

Sensitivity, specificity and predictive values of linear and nonlinear indices of heart rate variability in stable angina patients. *Int Arch Med* 2012;5:31.

50. Prabhakaran D, Jeemon P, Roy A. Cardiovascular Diseases in India Current Epidemiology and Future Directions. Circulation. 2016;133:1605–1620. DOI: 10.1161/CIRCULATIONAHA.114.008729.

51. Rajeev Sharma, Priti Kumari, Anita S. Malhotra. Evaluation and correlation of systolic time intervals (STI's) with autonomic functions in young adults. Int J Biol Med Res. 2012;3(4):2588-2592.

52. Reant P, Dijos M, Dona E, Mignot A, Ritter P, Bordachar P, et al. Systolic time intervals as simple echocardiographic parameters of left ventricular systolic performance: correlation with ejection fraction and longitudinal two-dimensional strain. European Journal of Echocardiography. 2010;11:834–844. DOI:10.1093 /ejechocard/jeq084.

53. Reddy S, Bahl A, Talwar KK. Congestive heart failure in Indians: How do we improve diagnosis & management? Review article. Indian J Med Res. Nov 2010;132(5):549-560.

54. Roerecke M, Rehm J. Chronic heavy drinking and ischaemic heart disease: a systematic review and meta-analysis. Open Heart. Aug 6 2014;1(1):e000135. DOI:10.1136 /openhrt-2014-000135.

55. Sadaf S, Arifuddin MS, Rahman MZ, Hazari MA, Quadri SB (2020) Correlation of systolic and diastolic time intervals with demographic and anthropometric parameters in young adults. J Pract Cardiovasc Sci. 6:23-32.

56. Takase B, Kurita A, Noritake M, Uehata A, Maruyama T, Nagayoshi H, et al. Heart rate variability in patients with diabetes mellitus, ischemic heart disease, and congestive heart failure. Journal of Electrocardiology. April 1992;25(2):79-88. DOI: 10.1016/0022 0736(92)90112-D.

57. Tomiyama H, Nakayama T, Watanabe G, Shiojim K, Sakuma Y, Yamamoto A. Effects of short-acting and long-acting loop diuretics on heart rate variability in patients with chronic compensated congestive heart failure. Am Heart J March 1999;137:543-8.

58. U.S. Department of Health and Human Services. The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.

59. Ware J, Sherbourne CD. The MOS 36-Item short-form health survey (SF-36): Conceptual framework and item selection. Med Care.1992;30:473–83.

60. Weissler AM, Harris WS, Schoenfeld CD. Systolic intervals in heart failure men. Circulation. 1968;37(2):149-59. DOI: 10.1161/01.cir.37.2.149.

61. Weissler AM. Systolic time intervals. N Engl J Med. Feb 10 1977;296:321-324. DOI: 10.1056/NEJM197702102960607.

62. Wennerblom B, Lurje L, Solem J, Tygesen H, Udén, Vahisalo R, et al. Reduced Heart Rate Variability in Ischemic Heart Disease Is Only Partially Caused by Ischemia An HRV Study before and after PTCA. *Cardiology* 2000;94:146–151. doi: 10.1159/000047309.

63. Wennerblom B, Lurje L, Westberg S, Johansson M, Lomsky M, Vahisalo R, Hjalmarson A. Effects on heart rate variability of isosorbide-5-mononitrate and metoprolol in patients with recent onset of angina pectoris. Cardiology. 1998;89(2):87-93. doi: 10.1159/000006762. PMID: 9524008.
64. Wiley CR, Pourmand V, Thayer JF and Williams DP (2021) A Close Examination of the Use of Systolic Time Intervals in the Calculation of Impedance Derived Cardiac Autonomic Balance and Regulation. Front. Neurosci. 15:625276. doi: 10.3389/fnins.2021.62527.
65. Windham BG, Fumagalli S, Ble A, Sollers JJ, Thayer JF, Najjar SS, Griswold ME, Ferrucci L. The Relationship between Heart Rate Variability and Adiposity Differs for Central and Overall Adiposity. J Obes. 2012;2012:149516. doi: 10.1155/2012/149516. Epub 2012 May 9. PMID: 22649714; PMCID: PMC3357556.
66. Yadav RL, Yadav PK, Yadav LK, Agrawal K, Sah SK, Islam MN. Association between obesity and heart rate variability indices: an intuition toward cardiac autonomic alteration - a risk of CVD. Diabetes Metab Syndr Obes. 2017 Feb 17;10:57-64. doi: 10.2147/DMSO.S123935. PMID: 28255249; PMCID: PMC5322847.

# *PRESENTATIONS AND*

# *PUBLICATIONS*

# PRESENTATIONS AND PUBLICATIONS

***List of presentations:***

1. Smitha PS, Vinutha Shankar MS, Niranjan Reddy. Evaluation of Systolic time intervals as an index of left ventricular function in patients with ischemic heart disease using continuous Doppler echocardiography. **Oral Presentation** at **ICONBAP 2020**, an International e-conference organized by the Department of Physiology, Sikkim Manipal Institute of Medical Sciences from 5$^{th}$ to 7$^{th}$ October 2020.
2. Smitha PS, Vinutha Shankar MS, Kaviraja Udupa, Niranjan Reddy, Raveesha A. Alterations in Heart rate variability before and after percutaneous coronary intervention. **Oral presentation** at **ISSEMCON 2022**, the 1$^{st}$ International conference of the Indian society of Sports and Exercise Medicine titled "Athlete Health-Moving beyond Injuries" held at Saveetha Medical College, Chennai from 24/3/22 to 26/3/22.
3. Smitha PS, Vinutha Shankar MS, Kaviraja Udupa, Raveesha A, Niranjan Reddy. Prognostic Value of Heart Rate Variability in Acute Coronary Syndrome. **Poster presentation** at a National conference **APPICON 2021** titled "Confluence of Health Sciences" held at ESIC Medical College, Faridabad from 14/4/22 to 16/4/22.

The 6th Annual & 1st Virtual International Conference of
Basic And Applied Physiology
V-ICONBAP 2020

5th - 7th October 2020
Theme - Environmental Physiology
Organised by:- Department of Physiology,
Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim

CERTIFICATE OF PARTICIPATION

This certificate is awarded to

MS. SMITHA P S

for participating in the V-ICONBAP 2020 and has presented an e-paper (oral / poster presentation)

Sikkim Medical Council has granted 06 credit hours for delegates and 09 credit hours to the speakers.(SMC/2098/2020)

Patron in Chief
Lt. Gen. (Dr) Rajan S. Grewal
AVSM, VSM
VC, SMU

Patron
Brig. (Dr) V. K. Mehta
Dean, SMIMS

Organizing Chairman
Prof (Dr) J. M. Jadeja

Organizing Secretary
Prof. (Dr) Sanjay Kumar

SAVEETHA
MEDICAL COLLEGE AND HOSPITAL

ISSEM

1st International Conference of Indian Society of Sports and Exercise Medicine

ISSEMCON 2022

24th - 26th March 2022

CERTIFICATE OF PARTICIPATION

This is to certify that

Dr/Mr/Mrs/Ms Smitha

Presented a Paper/ Poster in the **ISSEMCON 2022**
conducted by the **Indian Society of Sports and Exercise Medicine**
on 24th-26th March at Saveetha Medical College and Hospital

**Title of Paper / Poster**
Alterations in Heart rate variability before and after percutaneous coronary intervention

**Dr. Hanjabam Barun Sharma**
President-ISSEM

**Dr. Dobson Dominic**
Organising Chairman - ISSEMCON 2022
Head of Sports Medicine & Sports Science - SMCH

**Dr. Sidharth Unnithan**
General Secretary-ISSEM


67th Annual National Conference of Association of Physiologists and Pharmacologists of India
APPICON 2021-22 (13th - 16th April 2022)
Confluence of Health Sciences
Certified Participation of
Ms. Smitha PS
for presentation on
Prognostic Value Of Heart Rate Variability In Acute Coronary Syndrome
in the Oral/Poster section is endorsed.
Department of Physiology & Pharmacology
ESIC Medical College & Hospital, Faridabad
Dr. Shivani Agarwal
Organizing Secretary
Dr. Asim Das
Organizing Chairperson
Dr. A.K Pandey
General Secretary
Delhi Medical Council has accorded 9 credit hours for APPICON 2021-22 vide Letter No. 3405/DMC/CME/16C/2/2022 dated 16/03/2022

***List of Publications:***

1. **Seetharam SP**, Shankar MS, Reddy N. A narrative review of clinical applications of systolic time intervals. J Pract Cardiovasc Sci 2022;8:1-8.
2. **Seetharam SP**, Shankar MS, Reddy N. Evaluation of systolic time intervals in patients of ischemic heart disease with clinical heart failure. J Pract Cardiovasc Sci 2022;8:84-9.
3. **Seetharam SP**, Shankar VMS, Udupa K, Reddy N, Raveesha A. Alterations in heart rate variability before and after percutaneous coronary intervention in patients with ischaemic heart disease. Indian J Physiol Pharmacol 2022;66:188-95. doi:10.25259/IJPP_228_2022.
4. **Pernaje Seetharam S**, Shankar Ms V, Udupa K, A R, Reddy N. Prognostic value of heart rate variability in acute coronary syndrome. J Basic Clin Physiol Pharmacol. 2022 Oct 4. doi: 10.1515/jbcpp-2022-0134. Epub ahead of print. PMID: 36194293
5. **Smitha PS**, Kaviraja Udupa, Vinutha Shankar. Systolic Time Intervals in Clinical Heart Failure. Asian Hospital and Healthcare Management Magazine. 11 Nov 2022; Issue 52. https://www.asianhhm.com/medical-sciences/systolic-time-intervals-clinical-heart-failure.
6. **Smitha PS**, Vinutha Shankar MS, Kaviraja Udupa, Raveesha A, Niranjan Reddy. An **Original article** titled "Quality of life in the first episode of the Acute coronary syndrome" submitted to Health and Quality of Life Outcomes – **Under review.**

***Awards and Training:***

1. Undergone **Online training** on **Powerlab, LabChart, and LtStation** by AD instruments from 25/03/2020 to 17/04/2020. Secured a **memento** for qualifying AD Instruments online test.
2. Undergone **training** on "**Autonomic Function tests**" at Autonomic Lab, Neurophysiology department, NIMHANS, B'lore under the supervision of Dr. Kaviraja Udupa, Additional Professor, and Dr. Sathyaprabha, Professor and Head, Neurophysiology department, NIMHANS from 08/02/2021 to 20/02/2021.

# *ANNEXURES*

# ANNEXURE-I

# PATIENT INFORMATION SHEET AND WRITTEN INFORMED CONSENT FORMS

**Date:**

**Name of the Organization:** Sri Devaraj Urs Medical College, Tamaka, Kolar

**Name of the Investigator and Department**: Smitha P S, Ph.D. Scholar, Department of Physiology, SDUMC, Tamaka, Kolar

**Name of the Supervisor and Department**: Dr. Vinutha Shankar, Professor, and Head, Department of Physiology, SDUMC, Tamaka, Kolar

**Name of the Associate Supervisor and Department**: Dr. Raveesha, Professor, and Head, Department of Medicine, R L Jalappa Hospital, Tamaka, Kolar

**Title**: Evaluation of Systolic Time intervals and Heart Rate Variability as indicators of Cardiac autonomic function among male Ischemic heart disease patients.

**Introduction**:

I am Smitha P S, the lead researcher of this study. I welcome you to the above-said research study. The information provided in this document will help you to participate or not to participate in this study. You may ask me about any doubts or misconceptions you have.

**Purpose of the research**:

Heart attack is the most common cardiovascular disease and most common burden. The most prominent risk factors for Myocardial Infarction are Old age, Smoking, Hypertension, Diabetes mellitus, and total cholesterol and high-density lipoprotein levels. Other risk factors include male sex, low levels of physical activity, a past family history, obesity, and alcohol

use. Many risk factors for heart attack are potentially modifiable, with the most important being tobacco smoking. Left ventricular dysfunction is a sequel/consequence of a heart attack and can progress toward heart failure in the long run. In such cases, it will be difficult for a Clinician to manage the disease progression.

The autonomic nervous system is a division of the peripheral nervous system that supplies smooth muscle and glands, and thus influences the function of internal organs. The autonomic nervous system is a control system that acts largely unconsciously and regulates bodily functions, such as the heart rate, digestion, respiratory rate, pupillary response, urination, and sexual arousal.

In addition, the assessment of health-related quality of life (HRQoL) is an important measure of a patient's recovery after an illness. Little is known about the HRQoL among acute coronary syndrome (ACS) patients.

Therefore, the present study is designed to evaluate the potential role of Systolic Time Intervals (STI) as a useful tool in diagnosing left ventricular dysfunction in patients with ischemic heart disease who will be willing to undergo percutaneous coronary intervention and to compare Systolic time intervals predictor accuracy with Heart rate variability measurements in evaluating the presence of Cardiac autonomic dysfunction among male ischemic heart disease patients. Furthermore among ACS patients, quality of life assessment will be done using a validated SF-12 health survey questionnaire post-PCI.

**Duration of the study**: 03 years

**Protocol for Study**:

The study will be approved by the central ethical committee. Details of the study will be explained to all the subjects & written informed consent will be taken.

A general Physical examination of the patient will be done. The height and weight of the recruited subjects will be measured.

Next, the Systolic & diastolic blood pressure will be measured.12-lead electrocardiogram recording of all subjects will be done.

For all the recruited subjects; in the supine position, during normal breathing, simultaneous recording of an electrocardiogram, pulsed-wave Doppler echocardiogram) and the recording of lead-II electrocardiogram (to measure systolic time intervals) will be done four times: that is before percutaneous coronary intervention (PCI), 24 hours post-PCI, 3- and 6-month post-PCI.

During heart rate variability measurements, exposure of subjects to too bright light or noise will be avoided & the room temperature will be maintained at 22℃ to 26℃. Subjects will be asked to refrain from wearing accessories (ring, watch) that may interfere with the accurate measurement. During the measurement, study subjects will be asked not to move or talk, close their eyes or fall asleep, because it will have an effect on the test variables. So we request you to cooperate. In addition, participants will be requested not to control their breathing intentionally and for experimentation.

In addition, for all the post-PCI patients; to assess health-related quality of life (HRQoL) Short-form 12 (SF-12) health survey questionnaire will be used. Accordingly, QoL scores (Physical component scores/PCS-12 and mental component scores/MCS-12) will be measured thrice: that is 1-month post-PCI/post-phase 2 cardiac rehabilitation, 3 months post-PCI, and 6 months post-PCI.

**Side effects**: No known, expected side effects will occur during the study period, and in such cases, suitable care will be provided.

**Risks/ discomforts / anticipated risk**: The procedure is not invasive. For any discomfort during the procedure, suitable care will be provided.

**Benefits:**

**Cases:** All the study subjects will be investigated free of cost. Physician consultation and assistance will be given by the PI. Advanced management if required beyond the facilities available at our center, referral center and assistance regarding the competent physician shall be extended by the PI. Psychological counseling and moral support will be extended by the PI to both study subjects and their relatives.

**For the Community:** The present study shall enable clinicians to identify the ischemic heart disease process at an earlier stage which will benefit the community.

**Confidentiality:**

Participant details will not be disclosed at any moment until & unless compelled by the law or court. Participation is purely voluntary basis of the study participant. The right to refuse or withdraw participation is purely voluntary and you may not be under any obligation to participate in this research, consequently, there won't be any variation in the medical services required for you.

There will be no costs to you from this test. I personally do these experiments (measurements of systolic time intervals and heart rate variability). I and our research team will let you know if you have any doubts at the time of registration. If you ever need a medical opinion, I certify that you will be guided by a hospital with more facilities.

If you have any doubts, contact the

**Principal researcher**: Smitha P S; Contact number: 9900489490 and email address: smithaps1@gmail.com

**Supervisor:** Dr. Vinutha Shankar MS Professor, and Head, Dept. of Physiology; Contact number: 9845065374

**Associate Supervisor**: Dr. Raveesha A Consultant Physician, Professor, and Head, Dept. of General Medicine, Contact number: 9448448353.

**Written Informed Consent**

**Title**: Evaluation of Systolic Time intervals and Heart Rate Variability as indicators of Cardiac autonomic function among male Ischemic heart disease patients.

I have understood the details of the research proposal and had the opportunity to discuss the details of the project and ask questions to clear any doubts. I hereby confirm to participate in this study and undergo the tests at the required intervals. I consent voluntarily to participate as a participant in this research.

I understand that I can withdraw my consent anytime if I so desire.

**Name of the Patient:**

**Signature/Thumb impression:**

**Address:**

**Email address:**

**Date:**

**Witnesses names and signatures:**

1. _____

2. _____

A copy of this Informed Consent Form has been provided to the participant.

**Signature of the Principal Investigator**

## ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

**ದಿನಾಂಕ:**

**ಸಂಸ್ಥೆಯ ಹೆಸರು**: ಶ್ರೀ ದೇವರಾಜ್ ಅರಸ್ ವೈದ್ಯಕೀಯ ಮಹಾವಿದ್ಯಾಲಯ, ಟಮಕ, ಕೋಲಾರ.

**ಸಂಶೋಧಕರ/ಅಧ್ಯಯನ ಮಾಡುವವರ ಹೆಸರು ಹಾಗೂ ವಿಭಾಗ**: ಸ್ಮಿತಾ.ಪಿ.ಎಸ್, ಪಿಎಚ್‌ಡಿ ವಿದ್ಯಾರ್ಥಿಸರು, ಅಂಗ ಕ್ರಿಯಾ ಶಾಸ್ತ್ರ ವಿಭಾಗ, ಎಸ್.ಡಿ.ಯು.ಎಂ.ಸಿ, ಟಮಕ, ಕೋಲಾರ.

**ಮಾರ್ಗದರ್ಶಕರು ಹಾಗೂ ವಿಭಾಗ**: ಡಾ|| ವಿನುತಾ ಶಂಕರ್.ಎಂ.ಎಸ್., ಪ್ರಾಧ್ಯಾಪಕರು ಹಾಗೂ ವಿಭಾಗದ ಮುಖ್ಯಸ್ಥರು, ಅಂಗ ಕ್ರಿಯಾ ಶಾಸ್ತ್ರ ವಿಭಾಗ, ಎಸ್.ಡಿ.ಯು.ಎಂ.ಸಿ, ಟಮಕ, ಕೋಲಾರ.

**ಸಹಮಾರ್ಗದರ್ಶಕರು ಹಾಗೂ ವಿಭಾಗ**: ಡಾ|| ರವೀಶ. ಎ.,ಪ್ರಾಧ್ಯಾಪಕರು ಹಾಗೂ ವಿಭಾಗದ ಮುಖ್ಯಸ್ಥರು, ಔಷಧ ಶಾಸ್ತ್ರ ವಿಭಾಗ, ಅರ್.ಎಲ್.ಜಾಲಪ್ಪಆಸ್ಪತ್ರೆ, ಟಮಕ, ಕೋಲಾರ.

**ಸಂಶೋಧನೆಯ/ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ:** ಹೃದಯರಕ್ತನಾಳ ಸಂಬಂಧಿ ಕಾಯಿಲೆಯ ಪುರುಷ ರೋಗಿಗಳಲ್ಲಿ ಹೃದಯದ ಸ್ವನಿಯಂತ್ರಿತ ಕ್ರಿಯೆಯ ಸೂಚಕಗಳಾಗಿ ಸಿಸ್ಟೊಲಿಕ್ ಸಮಯದ ಮಧ್ಯಂತರ ಮತ್ತು ಹೃದಯಬಡಿತ ವ್ಯತ್ಯಾಸದ ಮೌಲ್ಯಮಾಪನ. ಇದರ ಆಂಗ್ಲ ಶೀರ್ಷಿಕೆ: "Evaluation of Systolic Time intervals and Heart Rate Variability as indicators of Cardiac autonomic function among male Ischemic heart disease patients."

**ಪರಿಚಯ**: ನಾನು ಸ್ಮಿತಾ.ಪಿ.ಎಸ್, ಈ ಅಧ್ಯಯನದ ಪ್ರಮುಖ ಸಂಶೋಧಕಿ. ಮೇಲೆ ಹೇಳಿದ ಸಂಶೋಧನಾ ಅಧ್ಯಯನಕ್ಕೆ ನಾನು ನಿಮ್ಮನ್ನು ಸ್ವಾಗತಿಸುತ್ತೇನೆ. ಈಗ ಒದಗಿಸಲಾದ ಮಾಹಿತಿಯು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಅಥವಾ ಭಾಗವಹಿಸದೆ ಇರಲು ನೀವು ಸ್ವತಂತ್ರರಾಗಿರುತ್ತೀರಿ. ನೀವು ಹೊಂದಿರುವ ಯಾವುದೇ ಅನುಮಾನಗಳು ಅಥವಾ ತಪ್ಪುಕಲ್ಪನೆಗಳ ಬಗ್ಗೆ ನೀವು ನನ್ನನ್ನು ಕೇಳಬಹುದು. ನಾನು ನಿಮಗೆ ನಿಮ್ಮ ಸ್ವಂತ ಮಾತೃಭಾಷೆಯಲ್ಲಿ ಅರ್ಥವಾಗುವ ರೀತಿಯಲ್ಲಿ ತಿಳಿಯ ಪಡಿಸುತ್ತೇನೆ.

**ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ**:

ಹೃದಯಾಘಾತವು ಸಾಮಾನ್ಯವಾಗಿ ಹೃದಯರಕ್ತನಾಳಕ್ಕೆ ಸಂಬಧಿಸಿದ ಕಾಯಿಲೆ ಹಾಗೂ ತೊಂದರೆ. ಹೃದಯಾಘಾತಕ್ಕೆ ಕಾರಣವಾದ ಪ್ರಮುಖ ಅಪಾಯಕಾರಿ ಅಂಶಗಳೇನೆಂದರೆ: ಪುರುಷರು, ಕಡಿಮೆಮಟ್ಟದ ದೈಹಿಕ ಚಟುವಟಿಕೆಯುಳ್ಳವರು, ಕುಟುಂಬದ ಹಿನ್ನಲೆಹೊಂದಿದವರು, ಬೊಜ್ಜು, ಮತ್ತು ಮದ್ಯಪಾನ ಮಾಡುವವರು. ಹೃದಯಾಘಾತಕ್ಕೆ ಅನೇಕ ಅಪಾಯಕಾರಿ ಅಂಶಗಳು ಸಂಭಾವ್ಯವಾಗಿ ಮಾರ್ಪಡಿಸಬಹುದಾದವು. ಅವುಗಳಲ್ಲಿ

ಪ್ರಮುಖವಾದದ್ದು ತಂಬಾಕು ಸೇವನೆ. ಎಡಭಾಗದ ಹೃದಯದ ಅಸಹಜಕ್ರಿಯೆ ಹೃದಯಾಘಾತದ ಪರಿಣಾಮವಾಗಿದೆ ಮತ್ತು ಇದು ಧೀರ್ಘಾವದಿಯಲ್ಲಿ ಹೃದಯವೈ ಫಲ್ಯದತ್ತಸಾಗಬಹುದು. ಅಂತಹ ಸಂಧರ್ಭದಲ್ಲಿ, ರೋಗಿಯ ಪ್ರಗತಿಯನ್ನು ನಿರ್ವಹಿಸಲು ವೈದ್ಯರಿಗೆ ಕಷ್ಟವಾಗುತ್ತದೆ.

ಸ್ವನಿಯಂತ್ರಿತ ನರಮಂಡಲವು ನರಮಂಡಲದ ಒಂದು ವಿಭಾಗವಾಗಿದ್ದು, ಅದು ಸ್ನಾಯು ಮತ್ತು ಗ್ರಂಥಿಗಳನ್ನು ನಿಯಂತ್ರಣ ಮಾಡುತ್ತದೆ ಮತ್ತು ದೇಹದ ಒಳಅಂಗಗಳ ಕಾರ್ಯಚಟುವಟಿಕೆಗಳ ಮೇಲೆ ಪ್ರಭಾವ ಬೀರುತ್ತದೆ. ಸ್ವನಿಯಂತ್ರಿತ ನರಮಂಡಲವು ಮನುಷ್ಯರ ಅರಿವಿಗೆಬಾರದೆ ಕಾರ್ಯನಿರ್ವಹಿಸುತಿರುತ್ತದೆ ಮತ್ತು ದೈಹಿಕ ಕಾರ್ಯಗಳನ್ನು ನಿಯಂತ್ರಿಸುತ್ತದೆ, ಉದಾಹರಣೆಗೆ ಹೃದಯಬಡಿತ, ಜೀರ್ಣಕ್ರಿಯೆ, ಉಸಿರಾಟದ ಪ್ರಮಾಣ, ಮೂತ್ರವಿಸರ್ಜನೆ, ಮತ್ತು ಲೈಂಗಿಕ ಪ್ರಚೋದನೆಯ ನಿರ್ವಹಣೆ.

ಹೆಚ್ಚುವರಿಯಾಗಿ, ಆರೋಗ್ಯ ಸಂಬಂಧಿತ ಜೀವನದ ಗುಣಮಟ್ಟದ ಮೌಲ್ಯಮಾಪನ (HRQoL) ಅನಾರೋಗ್ಯದ ನಂತರ ರೋಗಿಯ ಚೇತರಿಕೆಯ ಪ್ರಮುಖ ಅಳತೆಯಾಗಿದೆ. ರಕ್ತಕೊರತೆ ಹೃದ್ರೋಗಿಗಳಲ್ಲಿ HRQoL ಬಗ್ಗೆ ಸ್ವಲ್ಪ ತಿಳಿದಿದೆ.

ಆದ್ದರಿಂದ, ಪ್ರಸ್ತುತ ಅಧ್ಯಯನವನ್ನು ಎಡಭಾಗದ ಹೃದಯದ ಅಸಹಜ ಕ್ರಿಯೆಯುಳ್ಳ ರೋಗಿಗಳಲ್ಲಿ, ಎಡಭಾಗದ ಹೃದಯದ ಅಸಹಜಕ್ರಿಯೆಯನ್ನು ಪತ್ತೆಹಚ್ಚಲು, ಪರಿಧಮನಿಯ ಹಸ್ತಕ್ಷೇಪಕ್ಕೆ ಒಳಗಾಗಲು ಯಾರು ಸಿದ್ಧರಿರುತ್ತಾರೋ ಮತ್ತು ರಕ್ತಕೊರತೆ ಹೃದ್ರೋಗಿಗಳಲ್ಲಿ ಹೃದಯದ ಸ್ವನಿಯಂತ್ರಿತ ಅಸಹಜಕ್ರಿಯೆಯ ಉಪಸ್ಥಿತಿಯನ್ನು ಮೌಲ್ಯಮಾಪನ ಮಾಡುವಲ್ಲಿ ಸಿಸ್ಟೊಲಿಕ್ ಸಮಯದ ಮಧ್ಯಂತರಗಳ ಮುನ್ಸೂಚಕ ನಿಖರತೆಯನ್ನು ಹೃದಯಬಡಿತ ವ್ಯತ್ಯಾಸದ ಮಾಪನಗಳೊಂದಿಗೆ ಹೋಲಿಸುವುದರ ಜೊತೆಗೆ, ಈ ಪರೀಕ್ಷಾ ವಿಧಾನವನ್ನು ವಿನ್ಯಾಸಗೊಳಿಸಲಾಗಿದೆ. ಇದಲ್ಲದೆ ರಕ್ತಕೊರತೆ ಹೃದ್ರೋಗಿಗಳಲ್ಲಿ, ಪರಿಧಮನಿಯ ಹಸ್ತಕ್ಷೇಪದ ನಂತರದ ಮೌಲ್ಯೀಕರಿಸಿದ SF-12 ಆರೋಗ್ಯ ಸಮೀಕ್ಷೆಯ ಪ್ರಶ್ನಾವಳಿಯನ್ನು ಬಳಸಿಕೊಂಡು ಜೀವನದ ಗುಣಮಟ್ಟದ ಮೌಲ್ಯಮಾಪನವನ್ನು ಮಾಡಲಾಗುತ್ತದೆ.

**ಅಧ್ಯಯನದ ಅವಧಿ**: ಮೂರು ವರ್ಷಗಳು

**ವೈದ್ಯಕೀಯ ಅಧ್ಯಯನದ ಕಾರ್ಯವಿಧಾನ**:

ಅಧ್ಯಯನವನ್ನು ಕೇಂದ್ರ ನೈತಿಕ ಸಮಿತಿಯು ಅನುಮೋದಿಸುತ್ತದೆ. ಅಧ್ಯಯನದ ವಿವರಗಳನ್ನು ಎಲ್ಲಾ ರೋಗಿಗಳಿಗೆ ವಿವರಿಸಲಾಗುವುದು ಮತ್ತು ಲಿಖಿತ ಒಪ್ಪಿಗೆ ತೆಗೆದು ಕೊಳ್ಳಲಾಗುವುದು. ರೋಗಿಯ ಸಾಮಾನ್ಯ ದೈಹಿಕ ಪರೀಕ್ಷೆಯನ್ನು ಮಾಡಲಾಗುತ್ತದೆ. ರೋಗಿಗಳ ಎತ್ತರ ಮತ್ತು ತೂಕವನ್ನು ಅಳೆಯಲಾಗುತ್ತದೆ. ರಕ್ತದೊತ್ತಡವನ್ನು ನಿಖರಪಡಿಸಿಕೊಳ್ಳಲಾಗುತ್ತದೆ. ಎಲ್ಲಾ ರೋಗಿಗಳ ಎಲೆಕ್ಟ್ರೋಕಾರ್ಡಿಯೋಗ್ರಾಮ್ (ಇಸಿಜಿ) ಮೌಲ್ಯಮಾಪನವನ್ನು ಮಾಡಲಾಗುತ್ತದೆ.

ನೇಮಕಗೊಂಡ ಎಲ್ಲಾ ರೋಗಿಗಳಿಗೆ ಎಲೆಕ್ಟ್ರೋಕಾರ್ಡಿಯೋಗ್ರಾಮ್, ಎಕೋಕಾರ್ಡಿಯೋಗ್ರಾಮ್ ಮತ್ತು ಹೃದಯಬಡಿತ ವ್ಯತ್ಯಾಸದ ಮಾಪನದ ಅಳತೆಗಳನ್ನು ಮೂರುಬಾರಿ ಮಾಡಲಾಗುತ್ತದೆ: ಅಂದರೆ ಪರೀಕ್ಷೆಗೆ ಒಳಪಡುವಂಥಹ ಸಮಯದಲ್ಲಿ ಮೊದಲನೇಬಾರಿ, ಪರೀಕ್ಷೆಯ 24 ಗಂಟೆಗಳ ನಂತರ, ಮತ್ತು ಪಿಸಿಐನ 3-6 ತಿಂಗಳುಗಳ ನಂತರ. ಈ ಪರೀಕ್ಷೆಯು ಆಂಗ್ಲಭಾಷೆಯಲ್ಲಿ ಹೇಳುವಹಾಗೆ ಪೆರ್ಕ್ಯುಟೇನಿಯಸ್ ಪರಿಧಮನಿಯ ಹಸ್ತಕ್ಷೇಪದ ಮೂಲಕ ಮಾಡಲಾಗುವುದು.

ಮಲಗುವ ಭಂಗಿಯಲ್ಲಿ, ಸಿಸ್ಟೊಲಿಕ್ ಮಯದ ಮಧ್ಯಂತರಗಳ ಅಳತೆಗಳನ್ನು, ನಿರಂತರ ಇಸಿಜಿ ಮತ್ತು ಎಕೋಕಾರ್ಡಿಯೋಗ್ರಫಿಗಳ ಏಕಕಾಲಿಕ ರೆಕಾರ್ಡಿಂಗ್ ಮೂಲಕ ಮಾಡಲಾಗುತ್ತದೆ. ಮತ್ತು ಹೃದಯಬಡಿತದ ವ್ಯತ್ಯಾಸದ ಅಳತೆಗಳನ್ನು, ಇಸಿಜಿ ಮತ್ತು ಉಸಿರಾಟದ ಏಕಕಾಲಿಕ ರೆಕಾರ್ಡಿಂಗ್ ಮೂಲಕ ಮಾಡಲಾಗುತ್ತದೆ.

ನಮ್ಮ ಈ ಪ್ರಯೋಗದ ಸಮಯದಲ್ಲಿ, ರೋಗಿಗಳು ಹೆಚ್ಚು ಪ್ರಕಾಶಮಾನವಾದ ಬೆಳಕು ಅಥವಾ ಶಬ್ದಕ್ಕೆ ಒಡ್ಡಿಕೊಳ್ಳದಂತೆ ಎಚ್ಚರಿಕೆ ವಹಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಕೋಣೆಯ ಉಷ್ಣತೆಯನ್ನು 22°C ರಿಂದ 26°C ವರೆಗೆ ನಿರ್ವಹಿಸಲಾಗುತ್ತದೆ. ಮೌಲ್ಯಮಾಪನದ ಸಮಯದಲ್ಲಿ, ಅಧ್ಯಯನಕ್ಕೆ ಒಳಪಟ್ಟ ರೋಗಿಗಳು ಚಲಿಸಬಾರದು ಅಥವಾ ಮಾತನಾಡಬಾರದು, ಏಕೆಂದರೆ ಪರೀಕ್ಷೆಯ ಪರಿಣಾಮ ವ್ಯತ್ಯಾಸವಾಗುವುದು. ಕಣ್ಣುಮುಚ್ಚಬಾರದು ಅಥವಾ ನಿದ್ರಿಸಬಾರದು ಎಂದು ಕೇಳಾಲಾಗುತ್ತದೆ ಏಕೆಂದರೆ ಇದು ಸಹ ಪರೀಕ್ಷೆಯ ಪರಿಣಾಮದಲ್ಲಿ ವ್ಯತ್ಯಾಸವನ್ನು ಉಂಟುಮಾಡುತ್ತದೆ. ಆದ್ದರಿಂದ ದಯವಿಟ್ಟು ಸಹಕರಿಸಬೇಕಾಗಿ ಸವಿನಯ ಪ್ರಾರ್ಥನೆ. ಅವರು ಉದ್ದೇಶಪೂರ್ವಕವಾಗಿ ಉಸಿರಾಟವನ್ನು ನಿಯಂತ್ರಿಸಬಾರದು, ಬದಲಿಗೆ ಅದು ಸಾಮಾನ್ಯ ಮತ್ತು ವಿಶ್ರಾಂತಿ ಸ್ಥಿತಿಯಲ್ಲಿರಬೇಕು.

ಜೊತೆಗೆ, ಎಲ್ಲಾ ಪಿಸಿಐ ನಂತರದ ರೋಗಿಗಳಿಗೆ; ಆರೋಗ್ಯ ಸಂಬಂಧಿತ ಜೀವನದ ಗುಣಮಟ್ಟವನ್ನು ನಿರ್ಣಯಿಸಲು (HRQoL) ಶಾರ್ಟ್-ಫಾರ್ಮ್ 12 (SF-12) ಆರೋಗ್ಯ ಸಮೀಕ್ಷೆಯ ಪ್ರಶ್ನಾವಳಿಯನ್ನು ಬಳಸಲಾಗುತ್ತದೆ. ಅಂತೆಯೇ, QoL ಸ್ಕೋರ್‌ಗಳನ್ನು (ದೈಹಿಕ ಘಟಕ ಅಂಕಗಳು/PCS-12 ಮತ್ತು ಮಾನಸಿಕ ಘಟಕ ಅಂಕಗಳು/MCS-12) ಮೂರು ಬಾರಿ ಅಳೆಯಲಾಗುತ್ತದೆ: ಅಂದರೆ ಪಿಸಿಐನ 1 ತಿಂಗಳ ನಂತರ, ಪಿಸಿಐನ 3 ತಿಂಗಳ ನಂತರ, ಮತ್ತು ಪಿಸಿಐನ 6 ತಿಂಗಳುಗಳ ನಂತರ.

**ಪರಿಚಯವಿಲ್ಲದ ವಿಧಾನ**: ಭಾಗವಹಿಸುವವರಿಗೆ ಪರಿಚಯವಿಲ್ಲದಿದ್ದರೆ ಪರಿಚಯವಿಲ್ಲದ ವಿಧಾನಗಳನ್ನು ವಿವರಿಸಲಾಗುವುದು.

**ಅಪಾಯಗಳು / ಅಸ್ವಸ್ಥತೆಗಳು / ನಿರೀಕ್ಷಿತ ಅಪಾಯ**: ಯಾವುದೇ ತಿಳಿದ, ನಿರೀಕ್ಷಿತ ಅಡ್ಡಪರಿಣಾಮಗಳು ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಕಂಡುಬರುವುದಿಲ್ಲ ಮತ್ತು ಅಂತಹ ಸಂಧರ್ಭದಲ್ಲಿ ಸೂಕ್ತವಾದ ಆರೈಕೆಯನ್ನು ಒದಗಿಸಲಾಗುತ್ತದೆ.

**ಪ್ರಯೋಜನಗಳು:**

ಹೃದಯ ವೈಫಲ್ಯದ ಕಡೆಗೆ ಹೃದಯರಕ್ತನಾಳ ಸಂಬಂಧಿ ಕಾಯಿಲೆಯುಳ್ಳ ರೋಗಿಗಳಲ್ಲಿ, ಕಾಯಿಲೆಯ ಪ್ರಗತಿಯ ನಿರ್ವಹಣೆಯಲ್ಲಿ ಇದು ಪ್ರಯೋಜನ ಕಾರಿಯಾಗಬಹುದು. ಸ್ವನಿಯಂತ್ರಿತ ಕ್ರಿಯೆಯ ಅನುಸರಣಾ ಮೌಲ್ಯಮಾಪನವು ಚೇತರಿಕೆಯ ಸ್ಥಿತಿಯ ಬಗ್ಗೆ ಮಾಹಿತಿಯನ್ನು ಒದಗಿಸಬಹುದು.

**ಸಮುದಾಯ:** ಸಿಸ್ಟೊಲಿಕ್ ಸಮಯದ ಮಧ್ಯಂತರಗಳ ಅಳತೆ ಮತ್ತು ಹೃದಯಬಡಿತದ ವ್ಯತ್ಯಾಸದ ಅಳತೆಗಳ ಮೇಲ್ವಿಚಾರಣೆಯು, ಹೃದಯರಕ್ತನಾಳ ಸಂಬಂಧಿ ಕಾಯಿಲೆಯುಳ್ಳ ರೋಗಿಗಳಲ್ಲಿ ಮತ್ತು ಸಾಮಾನ್ಯ ಆರೋಗ್ಯವಂತಜನರಲ್ಲಿ, ಹೃದಯ ಸ್ವಾಯತ್ತ ಅಸಹಜಕ್ರಿಯೆಯ ಉಪಸ್ಥಿತಿಯನ್ನು ತನಿಖೆಮಾಡಲು ಸಹಾಯಮಾಡಬಹುದು.

**ಗೌಪ್ಯತೆ**: ಭಾಗವಹಿಸುವವರ ವಿವರಗಳನ್ನು, ಕಾನೂನು ಅಥವಾ ನ್ಯಾಯಾಲಯವು ಒತ್ತಾಯಿಸದ ಹೊರತು ಯಾವುದೇ ಕ್ಷಣದಲ್ಲಿ ಬಹಿರಂಗಪಡಿಸುವುದಿಲ್ಲ. ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು ನಿರಾಕರಿಸುವ ಅಥವಾ ಹಿಂತೆಗೆದುಕೊಳ್ಳುವ ಹಕ್ಕು ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ ಮತ್ತು ನೀವು ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಭಾಗವಹಿಸಲು ಯಾವುದೇ ರೀತಿಯ ಬಲವಂತವಿರುವುದಿಲ್ಲ ಹಾಗೂ ನಿಮ್ಮ ವೈದ್ಯಕೀಯ ಸೇವೆಗಳಲ್ಲಿ ಯಾವುದೇ ವ್ಯತ್ಯಾಸವಾಗುವುದಿಲ್ಲ. ನಿಮಗೆ ಈ ಪರೀಕ್ಷೆಯಿಂದ ಯಾವುದೇ ಖರ್ಚುವೆಚ್ಚಗಳಿರುವುದಿಲ್ಲ. ನಾನೇ ಖುದ್ದಾಗಿ ಈ ಪ್ರಯೋಗಗಳನ್ನು (ಸಿಸ್ಟೊಲಿಕ್ ಸಮಯದ ಮಧ್ಯಂತರಗಳ ಅಳತೆ ಮತ್ತು ಹೃದಯಬಡಿತದ ವ್ಯತ್ಯಾಸದ ಅಳತೆ) ಮಾಡುತ್ತೇನೆ. ಈ ಪರೀಕ್ಷೆಯ ನೋಂದಣಿ ಸಮಯದಲ್ಲಿ, ನಿಮಗೆ ಯಾವುದೇ ಅನುಮಾನಗಳಿದ್ದರೂ, ನಾನು ಹಾಗು ನಮ್ಮ ಪರೀಕ್ಷಾತಂಡ ತಿಳಿಯಪಡಿಸುತ್ತೇವೆ. ಇನ್ನು ಹೆಚ್ಚಾಗಿ ನಿಮಗೇನಾದರು ವೈದ್ಯಕೀಯ ಅಭಿಪ್ರಾಯಬೇಕಾದಲ್ಲಿ, ಇನ್ನು ಹೆಚ್ಚಿನ ಸೌಲಭ್ಯವಿರುವ ಆಸ್ಪತ್ರೆಯನ್ನು ನಿಮಗೆ ಮಾರ್ಗದರ್ಶನ ನೀಡುತ್ತೇನೆಂದು ಪ್ರಮಾಣೀಕರಿಸುತ್ತೇನೆ.

ನಿಮಗೆ ಯಾವುದೇ ಸಂದೇಹಗಳಿದ್ದರೆ, ಪ್ರಧಾನ ಸಂಶೋಧಕರನ್ನು ಅಥವಾ ಸಹ ಮಾರ್ಗದರ್ಶಕರನ್ನು ಸಂಪರ್ಕಿಸಿ.

**ಪ್ರಧಾನ ಸಂಶೋಧಕರ ಹೆಸರು**: ಸ್ಮಿತಾ.ಪಿ.ಎಸ್., ದೂರವಾಣಿ ಸಂಖ್ಯೆ: 9900489490 ಮತ್ತು ಇಮೇಲ್ ವಿಳಾಸ: smithaps1@gmail.com

**ಮಾರ್ಗದರ್ಶಕರ ಹೆಸರು:** ಡಾ|| ವಿನುತಾಶಂಕರ್.ಎಂ.ಎಸ್., ದೂರವಾಣಿ ಸಂಖ್ಯೆ: 9845065374

**ಸಹ ಮಾರ್ಗದರ್ಶಕರ ಹೆಸರು**: ಡಾ|| ರವೀಶ. ಎ., ದೂರವಾಣಿ ಸಂಖ್ಯೆ: 9448448353

## ಒಪ್ಪಿಗೆಪತ್ರ

**ಸಂಶೋಧನೆಯ / ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ:** ಹೃದಯರಕ್ತನಾಳ ಸಂಬಂಧಿ ಕಾಯಿಲೆಯುಳ್ಳ ರೋಗಿಗಳಲ್ಲಿ ಹೃದಯದ ಸ್ವನಿಯಂತ್ರಿತ ಕ್ರಿಯೆಯ ಸೂಚಕಗಳಾಗಿ ಸಿಸ್ಟೊಲಿಕ್ ಸಮಯದ ಮಧ್ಯಂತರ ಮತ್ತು ಹೃದಯ ಬಡಿತ ವ್ಯತ್ಯಾಸದ ಮೌಲ್ಯಮಾಪನ. ಇದರ ಆಂಗ್ಲಶೀರ್ಷಿಕೆ: "Evaluation of Systolic Time intervals and Heart Rate Variability as indicators of Cardiac autonomic function among male Ischemic heart disease patients."

ನಾನು ಸಂಶೋಧನೆಯ ವಿವರಗಳನ್ನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ ಮತ್ತು ಯೋಜನೆಯ ವಿವರಗಳನ್ನು ಚರ್ಚಿಸಲು ಮತ್ತು ಯಾವುದೇ ಅನುಮಾನಗಳನ್ನು ಬಗೆಹರಿಸಲು ನನಗೆ ಅವಕಾಶ ದೊರಕಿದೆ. ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಮತ್ತು ಅಗತ್ಯವಿರುವ ಸಮಯದಲ್ಲಿ ಪರೀಕ್ಷೆಗಳಿಗೆ ಒಳಗಾಗಲು ಸಿದ್ಧನಿದ್ದೇನೆಂದು ನಾನು ಈ ಮೂಲಕ ಧೃಡೀಕರಿಸುತ್ತೇನೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನಾನು ನನ್ನ ಸ್ವಂತ ಇಚ್ಛೆಯಿಂದ ಒಪ್ಪುತ್ತಿದ್ದೇನೆ.

ನಾನು ಬಯಸಿದರೆ ಯಾವಾಗ ಬೇಕಾದರೂ ನನ್ನ ಒಪ್ಪಿಗೆಯನ್ನು ಹಿಂಪಡೆಯಬಹುದು ಎಂಬುದನ್ನೂ ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

**ರೋಗಿಯ ಹೆಸರು:**

**ಸಹಿ / ಹೆಬ್ಬೆಟ್ಟು:**

**ವಿಳಾಸ:**

**ಇಮೇಲ್ ವಿಳಾಸ:**

**ದಿನಾಂಕ:**

**ಸಾಕ್ಷಿಗಳ ಹೆಸರು ಹಾಗು ಸಹಿ:**

೧._____

೨. _____

ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವವರಿಗೆ ಈ ಸಮ್ಮತಿ ಪತ್ರದ ನಕಲನ್ನು ಒದಗಿಸಲಾಗಿದೆ.

**ಪ್ರಧಾನ ಸಂಶೋಧಕರ ಸಹಿ**

## ANNEXURE-II

### Health-related Quality of life Short-form 12 questionnaire

(SF-12 Health Survey)

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer each question by choosing just one answer. If you are unsure how to answer a question, please give the best answer you can.

**1. In general, would you say your health is**:

□1 Excellent □2 Very good □3 Good □4 Fair □5 Poor

**The following questions are about activities you might do during a typical day. Does <u>your health now</u><u>limit you</u> in these activities? If so, how much?**

| | **YES, limited a lot** | **YES, limited a little** | **NO, not limited at all** |
|---|---|---|---|
| **2. Moderate activities** such as moving a table, pushing a vacuum cleaner, bowling, or playing golf. | □1 | □2 | □3 |
| **3.** Climbing **several** flights of stairs. | □1 | □2 | □3 |

**During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regulardaily activities <u>as a result of your physical health</u>?**

| | YES | NO |
|---|---|---|
| **4. Accomplished less** than you would like. | □1 | □2 |
| **5.** Were limited in the **kind** of work or other activities. | □1 | □2 |

**During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regulardaily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious)?**

| | YES | NO |
|---|---|---|
| **6. Accomplished less** than you would like. | □1 | □2 |
| **7.** Did work or activities **less carefully than usual**. | □1 | □2 |

**8.During the <u>past 4 weeks</u>, how much <u>did pain interfere</u> with your normal work (including work outsidethe home and housework)?**

□1 Not at all □2 A little bit □3 moderately □4 Quite a bit □5 Extremely

**These questions are about how you have been feeling during the <u>past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling.How much of the time during the <u>past 4 weeks</u>…**

| | All of the time | Most of the Time | A good bit of the time | Some of the time | A little of the time | Noneof the time |
|---|---|---|---|---|---|---|
| **9.** Have you felt calm & | □1 | □2 | □3 | □4 | □5 | □6 |

peaceful?

| | | | | | | |
|---|---|---|---|---|---|---|
| **10.** Did you have a lot of energy? | □1 | □2 | □3 | □4 | □5 | □6 |
| **11.** Have you felt down-hearted and blue? | □1 | □2 | □3 | □4 | □5 | □6 |

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**12**. **During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional problems</u>interfered with your social activities (like visiting friends, relatives, etc.)?**

□1 All of the time □2 Most of the time □3 Some of the time

□4 A little of the time □5 None of the time

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Patient name: Date: PCS: MCS:

Visit type (circle one)

Preop 6 week 3 month 6 month 12 month 24 month Other:_____

# ANNEXURE III

## PROFORMA

**Date:**

**Title:** Evaluation of Systolic time intervals and Heart rate variability as indicators of Cardiac autonomic function among male Ischemic heart disease patients

**General Physical Examinations:**

1. Patient ID:
2. Name of the Subject:
3. Address with Contact number:
4. Age/ Gender: years/
5. Occupation: Employed/Unemployed
6. Height: cm
7. Weight: kgs
8. Blood Pressure (SBP/DBP): mm Hg
9. PICCLE:
10. COVID-19: Positive/Negative; Test done/Not done

**History of** (personal and clinical): **risk factors for IHD**

- Killip classification of MI: Class I/Class II/Class III/Class IV
- Cigarette Smoking/Beedi: Yes/No; H/O or Current smoker: 1/5/10 cigarettes/day; Duration:
- Tobacco chewing:
- Alcohol consumption: yes/no; H/O or Current alcoholic: H/O or Current alcoholic: >5 units (One unit equals 10ml or 8g of pure alcohol, which is around the amount of

alcohol the average adult can process in an hour) of alcohol daily – sustained for 3 months duration

- Exercise: Yes/No; Physically active: Yes/No
- Pain score:
- Chest pain: Location-score: 0-1 (No pain)/1-3 (Mild)/4-7 (Moderate)/8-10 (Severe)
- Dyspnea: Yes/No
- Heartburn: Yes/No
- Psychological: anxious/depressed/angry/suicidal/homicidal
- Diabetes mellitus: Yes/No
- Hypertension: Yes/No
- Cardiac disease: Yes/No

➢ **Medications:**

- On β-blockers: Yes/No
- On vasodilators: Yes/No
- On calcium channel blockers:
- On ACE inhibitors: Yes/No
- On angiotensin II receptor blockers/Antagonists: Yes/No
- On oral hypoglycemic agents/Insulin: Yes/No
- On Statins: Yes/No
- On anticholinergics: Yes/No
- On diuretics: Yes/No
- On anti-thyroid drugs: Yes/No
- On thyroid hormone supplements: Yes/No
- On anticoagulants: Yes/No
- On antiplatelets: Yes/No

- On blood thinners: Yes/No
- On nitrates: Yes/No
- On cardiac glycosides: Yes/No
- On antacids: Yes/No
- On hematinics: Yes/No
- On multivitamins: Yes/No

➢ **Self-reported:**

- Depression: Yes/No
- Psychosis: Yes/No
- Rheumatic heart disease: Yes/No
- Parkinson's disease: Yes/No
- Multiple sclerosis: Yes/No
- Rheumatoid arthritis: Yes/No
- Systemic lupus erythematosus: Yes/No
- Psoriasis & psoriatic arthritis: Yes/No
- Amyloidosis: Yes/No
- Malignancy: Yes/No
- Anxiety: Yes/No
- Stress: Yes/No

**Family history:** Significant/Not significant

**12-lead ECG findings:**

- Heart rate: bpm
- STEMI/NSTEMI:
- Atrial fibrillation: Present/Absent

- Supraventricular tachycardia: Present/Absent

**2D-Transthoracic echo report: Pulsed wave Doppler findings**

- IHD:
- Chamber dimensions: Normal/Abnormal
- RWMA: Yes/No
- EDDd: mm, ESDd: mm Stroke volume: ml
- Fractional shortening: %
- MR: Trivial/Mild (Grade I)/Moderate(Grade II)/Severe (Grade III)
- LV systolic function: Normal/ Preserved/Mild LV systolic dysfunction/Moderate LVSD
- TR: Trivial/Mild/Moderate/Severe
- AR: Trivial/Mild/Moderate/Severe
- E/A ratio = E>A (Normal) / A>E (2:1) (Impaired) / E>A (Pseudo normal) / E>>A (3:1)
- Diastolic dysfunction: Grade I /Grade II /Grade III
- Clot/veg/P.E.: Yes/No
- LVEF: %

**I. Systolic time intervals: (5-lead ECG & pulsed Doppler Echo)**

1. Pre-ejection period (PEP): ms
2. Left ventricular ejection time (LVET): ms
3. Total electro-mechanical systole ($QS_2$): ms

**II. Heart rate variability measurements:**

- Time domain parameters:

1. SDNN: ms
2. RMSSD: ms
3. NN50:
4. pNN50: %

- Frequency domain parameters:

1. Total power: $ms^2$
2. Low frequency (LF) power: $ms^2$
3. High frequency (HF) power: $ms^2$
4. LF norm:
5. HF norm:
6. LF/HF ratio:

**III. Quality of Life (QoL) assessment using a Short form-12 health survey questionnaire**

1. PCS-12 score:
2. MCS-12 score:

# *RECOMMENDATIONS*

# RECOMMENDATIONS

## FURTHER RESEARCH

1. **Histological and immunohistochemical study:** The myocardial tissue could be harvested during the autopsy, for the immunohistochemical study. Myocardial fragments could be analyzed for the occurrence of infarct/interstitial fibrosis and LV performance.

2. Patients undergoing revascularization for IHD may experience less anxiety if they are given better pre-procedural information on coronary intervention or pharmaceutical methods. Further research might be done to understand how yoga and exercise training could affect the cardiac autonomic balance in these patients as potential future directions.

## FUTURE IMPLICATIONS

Since the study showed significant changes in STIs (PEP and PEP/LVET) and short-term linear HRV indices (SDNN, rMSSD, HF, and TP) after successful revascularization with PCI in patients who had MACE implied that this surgical treatment might have altered the cardiac autonomic balance. Hence, future studies/clinicians might consider using these metrics as prognostic indicators.