7-1-2015

ASSOCIATION BETWEEN LEFT VENTRICULAR EJECTION FRACTION (LVEF) IN PATIENTS WITH REGIONAL ISCHEMIA AND INFARCTION ON MYOCARDIAL PERFUSION IMAGES

Alireza Esfahane

Alireza B. Esfahane

Candidate

Internal Medicine

Department

This thesis is approved, and it is acceptable in quality and form for publication:

Approved by the Thesis Committee:

Cameron Crandall, M.D., Ph.D., Chairperson

Abass Alavi, M.D.

Denece Kesler, M.D., MPH

Herbert Davis, Ph.D.

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By

ALIREZA B. ESFAHANE

M.D., Tehran University of Medical Sciences, 1997

THESIS

Submitted in Partial Fulfillment of the
Requirements for the Degree of

Master of Science -Biomedical Sciences

The University of New Mexico
Albuquerque, New Mexico

July, 2015

DEDICATION

This thesis is dedicated to my family

ACKNOWLEDGEMENTS

Foremost, I would like to express my sincere gratitude to my mentor Dr. Alavi for helping me through this research with the continuous support of my study, for his patience, motivation, enthusiasm, and immense knowledge. His guidance helped me throughout the research and writing of this thesis. I could not have had a better advisor and mentor for my master study.

In addition to my mentor, I would like to thank the rest of my advisory committee: Dr. Crandall, Dr. Davis and Dr. Kesler, for their encouragement, insightful comments, and hard questions.

My sincere thanks also go to my prior program director, Dr. Hankins for training me as a nuclear medicine physician. He was a wonderful teacher to me and helped me to collect the data for this study.

I would like to express my gratitude to all of the Department faculty members for their help and support.

I would also like to thank my family for the support that they provided me throughout my entire life.

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Alireza B. Esfahane

M.D., Tehran University of Medical Sciences, 1997
Master of Science -Biomedical Sciences, University of New Mexico, 2015

ABSTRACT

OBJECTIVES: We used gated single-photon emission computed tomography Technetium (99mTc) tetrofosmin (SPECT Myoview), myocardial perfusion imaging (MPI) to (i) determine whether the location of myocardial infarction and Ischemia affect left ventricular function, and (ii) associated changes between post-stress (SEF) and rest ejection fraction (REF) with segmental perfusion abnormalities.

METHODS: Five hundred ninety-eight patients underwent a rest- stress or stress–rest gated SPECT Myoview. A Quantitative Gated SPECT (QGS) software program was used to calculate the left ventricular ejection fraction at rest and stress. The left ventricle was divided into thirteen segments. The perfusion abnormalities on each segment were visually assessed. The patients' scans were divided into 4 groups with ischemia, infarction, artifact and no findings on scans. Associations between the segments and SEF, REF were studied.

[1] Alireza B. Esfahane, University of New Mexico; Cameron Crandall, University of New Mexico; Herbert Davis, University of New Mexico; Denece Kesler, University of New Mexico, Jordan H. Hankins, University of Nebraska Medical Center; Abass Alavi, University of Pennsylvania.

RESULTS: Patients with artifact showed no statistically significant association with decrease in either REF or SEF at any segments. Multiple segments among the patients with infarction showed association with REF or SEF including; anterior apical segment (REF p 0.039, Coeff – 10.07) apex (REF p 0.000, Coeff – 4.83), mid septal segment (SEF p 0.011, Coeff -18.61), anterior apical segment (SEF p 0.032, Coeff -9.93), apical lateral segment (SEF p 0.035, Coeff – 11.45) and apex (SEF p0.000, Coeff -5.48). The patients with ischemia showed only association with SEF on the mid septal segment (SEF p 0.038, Coeff -10.50).

CONCLUSION: The segmental perfusion abnormality showed significant association with REF and SEF mostly after myocardial infarction. In this group, 4 out of 13 segments showed significant association with decreasing LVEF. Only the anterior apical segment and apex showed an association with REF while the anterior and lateral apical segments, mid septal and apex showed significant association with decreasing SEF after infarction. No significant association between any segments involved in artifact and LVEF were identified but ischemia showed association only with SEF if mid septal segment was involved. The global LVEF is the most affected by the mid septal segment in myocardial infarction. The overall results suggested that some of the segments of the infarction are more associated with decreasing LVEF compared to the other segments of the myocardium.

Keywords: gated SPECT Myoview, left ventricular function, myocardial infarction, perfusion abnormalities

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INTRODUCTION

More than 5 million people in the United States have heart failure (HF). Sixty-two percent of HF is secondary to ischemic heart disease and has an overall annual mortality rate of 10% (1). Treatment of HF focuses on improving the symptoms and preventing the progression of the disease to disability or death. Reversible causes of HF by reperfusion therapy of the myocardium, which keeps the arteries open, need to be addressed (2). Categories of reperfusion therapy include thrombolytic drugs and procedures to open arteries with stents, or to graft arteries around blockages. These interventions have become central to the modern treatment of acute myocardial infarction (3). Without a timely reperfusion intervention, it is likely that the patient will experience complications such as heart failure if the damaged heart is no longer able to adequately pump blood around the body. Many studies have shown the cost effectiveness of heart failure prevention for screening, interventions and treatments [48, 49, 50]. Other important complications are: aneurysm or rupture of the myocardium and arrhythmias, ventricular fibrillation, ventricular tachycardia, atrial fibrillation, and heart blockage. Left Ventricular Ejection Fraction (LVEF) represents the volumetric fraction of blood that is pumped out of the left ventricle (heart) with each heartbeat or cardiac cycle. It indicates whether the heart is able to provide sufficient pump action to maintain blood flow to meet the needs of the body (4). LVEF is comprised of two components: 1) Rest Ventricular Ejection Fraction (REF) and 2) Stress Ventricular Ejection Fraction (SEF). HF is characterized by a decreased LVEF of less than 40%. Two main coronary arteries and their branches supply blood to the myocardium. The thickness of the myocardium differs according to the segment/region and the cardiac walls,

which is supplied by the coronary arteries. Myocardial perfusion abnormality (infarction/ischemia) decreases myocardial contractility and, as a result, diminishes cardiac output and leads to HF.

Prevention of cardiovascular diseases including heart failure is very important. The prevention is divided into three subcategories including primary prevention when no diagnosis of heart disease is confirmed and development of the disease is prevented by a healthy diet, physical activities, smoking cessation etc. The secondary prevention when the diagnosis of heart disease is confirmed by screening (still no clinical signs and symptoms of the disease) or by treatment of the disease. The tertiary prevention takes place after a heart attack is confirmed but when we want to prevent disability such as heart failure or death secondary to the disease. Myocardial perfusion imaging (MPI) often identifies perfusion abnormalities before clinical signs and symptoms of HF. It also facilitates the secondary and tertiary prevention of heart failure by identifying the region of perfusion abnormality as well as the severity and size of the perfusion defect.

MPI is a nuclear medicine procedure that illustrates the function of the myocardium by gated single-photon emission computed tomography (gated SPECT) (Figure 1). MPI is performed for diagnosing cardiac perfusion abnormalities such as cardiac ischemia and infarction, establishing prognosis, assessing the effectiveness of therapy, and evaluating myocardial viability. MPI helps to identify regional/segmental perfusion abnormalities, which reflect total ventricular functional impairment and estimate the true anatomic infarct size or perfusion defect. Software for automatic processing of gated SPECT images allows the analysis of several parameters of cardiac function, such as Left Ventricular Ejection

Fraction (LVEF), wall motion, wall thickening, ventricular volumes, and regional perfusion abnormalities [5,6]. The relative accuracy and reliability of gated SPECT has been established in comparison with the reference standard, such as magnetic resonance imaging or gated blood pool study [7,8].

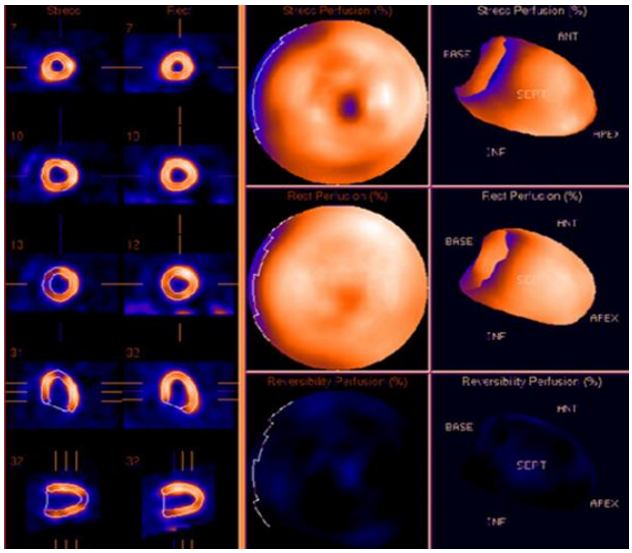

Figure 1: Tc-99m is used in myocardial perfusion imaging (i.e., comparing a 'rest' and 'stress' image to identify ischemia/infarction), avid infarct imaging (to detect damaged myocardial tissue post-MI) and cardiac function studies (to determine how well the heart is pumping via LVEF).

Acute myocardial ischemia/infarction rapidly impairs contractile function [29]. This dysfunction can persist for several hours after transient nonlethal ischemia but eventually is followed by full functional recovery [30]. In patients with coronary artery diseases (CAD), repeated episodes of ischemia may be a substrate for the development of chronic post-ischemic LV dysfunction [31, 32]. At present, there are no randomized controlled trial studies, but retrospective studies indicate that patients who undergo a preoperative assessment of ischemia/ infarction with myocardial viability have better in-hospital and 1-year outcomes when a viability test such as MPI is added to clinical and angiographic data

[33, 34]. Technical characteristics of each imaging modality have been reviewed by American Heart Association/American College of Cardiology scientific statements. MPI is a widely available modality with well-established clinical and prognostic validation. It helps to identify the segment(s)/region(s) of the heart with perfusion abnormalities, as well as the size and severity of the perfusion defects. MPI is also a powerful modality to identify the viable myocardial tissue after perfusion abnormalities and cardiac wall motion abnormalities. This information help providers to select the patients who benefit from reperfusion interventions, such as fibrinolytic drugs or stent placement and coronary artery bypass grafting (CABG). Myocardial revascularization and reperfusion interventions are appropriate when the expected benefits, in terms of survival or health outcomes (symptoms, functional status, and/or quality of life), exceed the expected negative consequences of the procedure.

Sobic-Saranovic and colleagues in 2009 found that global left ventricular function is significantly more affected after anterior MI in patients with reversible ischemia in addition to fixed wall defects. Several studies have shown that LVEF improved significantly (i.e., ≥5%) after revascularization in ≈60% of patients (range, 38% to 88%) [35, 36, 37, 38]. A meta-analysis [39] demonstrated an increase in LVEF in patients with evidence of ischemia/ infarction with viable myocardium. A general consensus exists that the changes in LVEF after revascularization are linearly correlated with the number of viable segments [35, 40, 41]. However; no study has been performed to correlate the location of segment(s)/region(s) of ischemia/ infarction with LVEF. Anterior infarctions show a lower LVEF than inferior or lateral ones of the same extent [42]. The relationship between

symptoms and the severity of the underlying disease is elusive. The magnitude of improvement in heart failure symptoms after revascularization in patients with ischemic cardiomyopathy seems to be related to the quantitative extent of myocardial ischemia/ infarction with viability [43]. The prognostic value of viability testing such as MPI and the impact of therapeutic choice for survival have been tested in a meta-analysis of 24 nonrandomized studies carried out between 1992 and 1999 which included 3088 patients with an LVEF <40%. The meta-analysis demonstrated a significant association between revascularization and improved survival rates in patients with LV dysfunction and evidence of myocardial viability independently of the imaging technique used [44, 45].

Sciagrà R et al, 2004, examined the relationships between infarct size and severity with LV ejection fraction (EF) and volumes in 215 myocardial infarction patients. Infarct size was expressed as LV percent, and infarct severity as the lowest activity ratio within the defect. LVEF was calculated with commercial software (see the methods section, below). There was a significant association between infarct size and LVEF ($r=-0.68$, $P<0.00001$). Slightly lower correlations were demonstrated using infarct severity. A significantly higher association was observed between infarct size and LVEF in anterior than in non-anterior infarctions ($r=-0.75$ vs. -0.60, $P<0.05$). Infarct size and severity correlate closely with LVEF derived from the MPI study.

LVEF performance can be diminished secondary to ventricular remodeling [9] which is due to the changes in the size, shape, structure and physiology of the heart after injury to the myocardium. [10] The injury is typically due to acute myocardial infarction or chronic

ischemia. Ventricular remodeling may result in diminished contractile (systolic) function and reduced stroke volume and LVEF.

Noninvasive cardiac imaging has become a worldwide utility enabling the study of cardiac performance reproducibly and inexpensively. Dedicated technology such as echocardiography, computed tomography (CT Scan), magnetic resonance imaging (MRI), radionuclide cardiac stress test gated SPECT (MPI) and radionuclide angiography (MUGA) scanning have definitively allowed clinically relevant software mathematics regarding ischemia, congenital heart disease, and heart failure. The relationship between left ventricular ejection fraction and infarct size assessed by MRI shows that infarct size by MRI can be used to estimate a maximum possible LVEF and a dysfunction [11].Myocardial perfusion scan (MPI) is a nuclear medicine procedure that illustrates the function of the myocardium.[5] MPI using cardiac rest and stress single-photon emission computed tomography (SPECT) with Technetium-99m (Tc-99m) based radiotracers is a common method for detecting flow-limiting coronary artery disease and can quantify regional and global ventricular function [7].

The cardiac stress test is done with heart stimulation, either by exercise on a treadmill, pedaling a stationary exercise bicycle ergometer [6] or with intravenous pharmacological stimulation, with the patient connected to an electrocardiogram (ECG). People who cannot use their legs may exercise with a bicycle-like crank that they turn with their arms. [6] For evaluation of cardiac function after stress, one popular method is the use of myocardial perfusion imaging (MPI). Millions of patients receive this kind of exam every year to evaluate cardiac perfusion abnormalities and function to prevent HF by performing

appropriate managements. Crucial to preventing HF, is the identification of the segment(s)/region(s) of the myocardium that will decrease LVEF the most after myocardial ischemia or infarction.

In patients with acute myocardial infarction, segmental wall motion abnormalities can be seen not only in the zone of acute infarction but also in regions of prior infarction and areas with ischemic “stunning” or “hibernation” of myocardium that is nonfunctional but still viable.[12,13,14, 16,17, 18] The estimation of infarct size by echocardiography [12] correlates modestly with thallium 201 perfusion defects,[14] peak creatine kinase levels,[13, 15] hemodynamic changes,[12] findings on ventriculography, [15] coronary angiography [16] and pathological findings.[19] However, it does predict the development of early [20] and late [21] complications and mortality.[12, 22] In a given patient with acute myocardial infarction, global and regional ventricular function, as well as clinical status, may improve (especially after reperfusion therapy) or can occasionally deteriorate. In general, more extensive perfusion abnormalities denote an increased risk of complications, including death, recurrent infarction, pump failure and serious ventricular dysrhythmias or heart block, even in patients who appear to be well clinically. [20, 23, 13, 17, 18, 20, 21]

Myocardial perfusion imaging (MPI) often identify perfusion abnormalities very early in the progression of heart failure before medical signs and symptoms are apparent or the heart failure is identified by other diagnostic tests. This early detection allows heart failure to be treated early in its course when there may be a more successful prognosis. Not only does MPI play a role in the secondary prevention of heart failure as explained earlier, but it is also important for secondary and tertiary prevention of heart failure by identifying the

region perfusion abnormality as well as the severity and size of the perfusion defect. This guides the management of patients for an appropriate therapy to reduce the negative impact of symptomatic disease, such as disability or death.

In patients with coronary artery disease, gated SPECT provides useful information about the extent and severity of reversible perfusion defects, regional wall motion abnormalities, global LV dysfunction, and the presence of post-ischemic or infarction LV dysfunction. (24)

Several studies have shown an added prognostic value of Rest Ejection Fraction (REF), Stress Ejection Fraction (SEF), end-systolic volume (ESV) over clinical and perfusion parameters for predicting cardiac death in patients with coronary artery disease [12–14]. However, data are limited regarding the gated SPECT post-stress global and regional LV functions in patients with a history of myocardial infarction and ischemia, particularly with the extent of perfusion abnormalities relative to the location of infarction and ischemia [9,15].

The last decade has witnessed extensive application of PET techniques to assess myocardial viability and has provided valuable information that is important in analyzing the risk: benefit ratio for several therapeutic measures. Recent advances in PET instrumentation and radiopharmaceuticals have generated considerable interest in using PET for evaluating an array of cardiovascular disease [51].

An important evolution has recently taken place in the field of cardiovascular Positron Emission Tomography (PET) imaging. It was originally a highly versatile research tool that has contributed significantly to advance our understanding of cardiovascular

physiology and pathophysiology, PET has gradually been incorporated into the clinical cardiac imaging portfolio contributing to the diagnosis and management of patients investigated for coronary artery disease (CAD). PET myocardial perfusion imaging (MPI) has an average sensitivity and specificity around 90% for the detection of angiographically significant CAD and is also a very accurate technique for the prognostication of patients with suspected or known CAD. In clinical practice, Rubidium-82 ((82)Rb) is the most widely used radiopharmaceutical for MPI that also affords accurate and reproducible quantification in absolute terms (ml/min/g) comparable to that obtained by cyclotron produced tracers such as Nitrogen-13 ammonia ((13)N-ammonia) and Oxygen-15 labeled water ((15)O-water). Quantification increases the sensitivity for detection of multi-vessel CAD and may also be helpful for the detection of early stages of atherosclerosis or microvascular dysfunction. PET imaging combining perfusion with myocardial metabolism using (18) F-Fluorodeoxyglucose ((18)F FDG), a glucose analog, is an accurate standard for the assessment of myocardial hibernation and risk stratification of patients with left ventricular dysfunction of ischemic etiology. It is helpful for guiding management decisions regarding revascularization or medical treatment and predicting improvement of symptoms, exercise capacity and quality of life post-revascularization. The strengths of PET can be increased further with the introduction of hybrid scanners, which combine PET with computed tomography (PET/CT) or with magnetic resonance imaging (PET/MRI) offering integrated morphological, biological and physiological information and hence, comprehensive evaluation of the consequences of atherosclerosis in the coronary arteries and the myocardium [52].

Vascular inflammation detected by FDG-PET/CT has been shown to predict cardiovascular (CV) events independent of traditional risk factors and is also highly associated with the overall burden of atherosclerosis. Plaque activity by FDG-PET/CT is modulated by known beneficial CV interventions such as short term (12 week) statin therapy as well as longer term therapeutic lifestyle changes (16 months) [53]. The early detection of atherosclerosis with (18) F-FDG PET may allow for the initiation of preventative interventions prior to the manifestation of significant structural abnormalities or symptoms of disease [54].

The purpose of this study was to evaluate whether segments/locations of perfusion abnormalities have a significant association with REF and SEF assessed by gated SPECT in patients with an infarction and ischemia. This finding may help to better understand how to select and prioritize patients for restoring coronary artery flow according to MPI findings to prevent HF.

METHODS

Study Population

Our research design is a cross-sectional study. We chose subjects by a convenience sampling method, searching the electronic health records (EHR) for patients who were referred for assessment of myocardial perfusion, coronary artery disease and LVEF by MPI. The study protocol was approved by the Ethics Committee, Institutional Review Board (IRB) of the University of Nebraska Medical Center (UNMC) and the University of New Mexico (UNM).

From January 2012 to December 2012, 701 patients underwent gated SPECT myocardial perfusion imaging (MPI) at the University of Nebraska Medical Center (UNMC). We excluded 105 (15%) of the subjects due to incomplete scans (if the patient had either a stress or rest scan only) or the scan interpretation was as equivocal or ischemia, infarction, and artifacts were identified on MPI, overlapped and it was difficult to separate the diseases. We selected from this group a total of 596 patients (mean age 66.0 ± 12 years, 65.7 men, and 66.3 women) (Table A-1). Based on the finding on MPI, the patients were divided into four groups of ischemia (237 patients), infarction (193 patients), artifact (166 patients) and no findings on scans (69 patients) (Tables 3 & 4). The subjects are adults who underwent either an exercise or pharmacological stress test using radionuclide Technetium (99mTc) tetrofosmin (Mayoview) [46]. The data from the picture archiving and communication system (PACS) regarding the MPI were assessed and recorded. We evaluated the MPI by reviewing images using the Xeleris workstation (GE Healthcare). We also collected information such as age, sex, BMI, family history of cardiovascular diseases,

documented coronary artery disease (CAD), DM, stent or CABG by searching EHR. These images were already performed and stored in the picture archiving and communication system (PACS). PACS is a medical imaging technology which provides economical storage of images and convenient access to images from multiple modalities. A minimum of two radiologists evaluated each MPI by reviewing images using the Xeleris workstation. Xeleris display, processing, archiving, and communication of data were acquired by emission tomography cameras used in diagnostic radiology, including procedures for planar imaging, whole body imaging, tomographic (SPECT) imaging, positron imaging by coincidence, attenuation correction, and anatomical image registration. We were able to transfer the images between PACS and Xeleris for analysis and assessment. For evaluation of regional perfusion abnormalities, we divided the human heart 2D images (MPI) into thirteen segments/regions (Figure 2) using the software Quantitative Gated SPECT QGS at 3 levels; base, mid and distal portion (excluding the apex). We then divided each level into four segments (anterior, lateral, inferior and septal) (Figure 2). The radiologists evaluated each segment using the software programs for myocardial perfusion abnormalities secondary to ischemia and infarction. The radiologist at UNMC evaluated each scan (stress and rest MPI) and recorded the segment numbers, which had involvement by ischemia, infarction, and artifact. For the evaluation of the LVEF, the radiologists considered all of the available results from the other imaging investigations such as prior MPI, cardiac catheterization (CC), cardiac echo (CE), laboratory data, and the clinical courses and compared them to LVEF calculated by the software programs. This evaluation was important to reduce the possibility of any technical errors. Association between segmental/regional perfusion

abnormalities and LVEF was evaluated by Quantitative Gated SPECT (QGS). For the computation of LVEF (REF and SEF), we used a widespread, commercially available automated Quantitative Gated SPECT algorithm (QGS; Cedars-Sinai Medical Center).

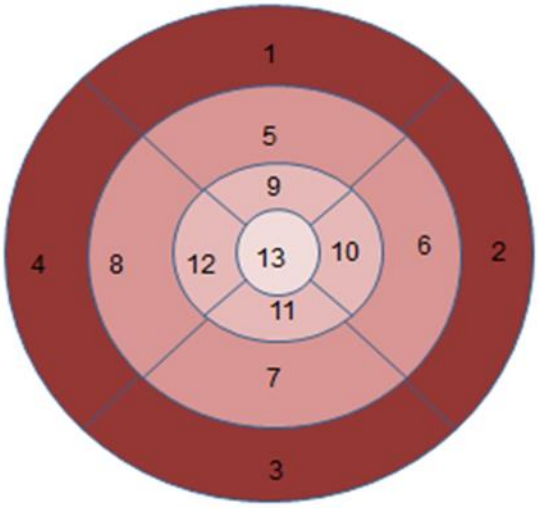

Figure 2: 2 D image of MPI Left Ventricle, which is divided into 13 segments.

Assessment and Data Acquisition

All of the patients underwent one day (weight<300 Ibs.) or two day (weight> 300 Ibs.) stress test protocols according to their weight. If the patients' weight was less than 300 pounds, the patient, after 4 hours of fasting, received an average 8-10mCi Tc99m Myoview (tetrofosmin) and rest scans were performed after approximately 1 hour. After the rest scan, patients underwent either exercise stress test protocols (Bruce or modified Bruce protocols) or received a pharmacological stress test using either adenosine (140 mcg/kg/min), dipyridamole (0.5 mg/kg/over 4 min), regadenoson (fixed dose 0.4mg) or dobutamine (beginning with 5-10mcg/kg/minute for 3 minutes and increase every 3 minutes to a maximum dose of 40 mcg/kg/min). During exercise or pharmacologic stress,

approximately 25-30 mCi Tc99m tetrofosmin (Myoview) [46] was administered to the patients. After approximately 30-40 minutes, the stress scans were performed.

If the patients weighed more than 300 Ibs., they underwent a two day scan protocol. First-day patients underwent a stress test with 30-45mCi Tc99m Myoview and if the scan showed any abnormality, the patients received a rest scan on the following day with 30-45mCi Tc99m Myoview. After completion of two scans (stress and rest), the images were transferred to Xeleris for processing with the software programs QGS. The Society of Nuclear Medicine Procedure Guidelines for Myocardial Perfusion Imaging were followed for all of the patients.

Gated SPECT Myoview data were acquired in the supine position with the dual-head SPECT – CT camera (GE Healthcare, USA) equipped with a high-resolution low-energy collimator. Sixty-four projection images with over 180 noncircular orbits were acquired. The time per projection was 20 seconds, matrix size 64 x 64, and gating eight frames per cardiac cycle.

Data Reconstruction and Image Analysis

Using the QGS commercial software, raw images/data were generated from gated projection data, reconstructed with a filtered back-projected algorithm, and reoriented to obtain oblique-angle tomograms parallel to the long and short axes of the left ventricle. The reconstructed data were projected as myocardial tomographic slices in the short axis, vertical long axis, and horizontal long axis views. Gated SPECT Myoview data were then processed and analyzed using QGS software.

The myocardium was divided into 13 segments, 3 segments for each anterior, inferior, lateral and septal walls plus a segment for the apex.

The assessment of the regional perfusion abnormality was performed by visual inspection of gated SPECT-CT perfusion images. The REF and SEF were calculated by QGS.

Study Models

We created four models for assessment of the segments, cardiac walls and LVEF. The first model was designed for the evaluation of REF and SEF (dependent variables) for each of the 13 segments individually in the groups of patients with ischemia, infarction, and artifact. For this purpose, each one of the segments (13 segments) was evaluated separately for association with REF and SEF in each group of patients (Tables 4 and 5). The second model was designed to evaluate REF and SEF if any of the segments were involved in perfusion abnormalities in each cardiac wall (anterior, lateral, inferior and septal walls). This model was tested for the mean of REF and SEF for each cardiac wall in each group of patients separately. A mean of REF and SEF of each cardiac wall was calculated, if any or more than one of the 3 segments were involved in perfusion abnormalities (OR) (Tables A-3 and A-4). The third model was designed similar to the second model except that all 3 segments had to be involved in perfusion abnormalities together (AND) (Tables A-5 and A-6). The fourth model was designed for the evaluation of the association of each of the 13 segments (dependent variables) individually with REF and SEF in the groups of patients with ischemia, infarction, and artifact. For this purpose, each one of the segments (13 segments) was evaluated separately for association with REF and SEF in each group of patients.

Statistical Analysis

Our primary analysis tests the underlying probability of "if the anterior segment(s)/region(s) of ischemia and infarction have a greater association with LVEF when compared to other areas of infarction/ischemia." (HO= anterior wall perfusion abnormality doesn't affect LVEF more than the other cardiac wall's segments, HI = anterior wall perfusion abnormality affects LVEF more than the other cardiac wall's segment,). We assumed that some of the cardiac segments' perfusion abnormalities decrease LVEF more than the others. We include calculations for two kinds of perfusion abnormalities; ischemia and infarction. As mentioned earlier, we also selected two additional groups with no findings on scans and the scans, which read as artifacts with no perfusion abnormalities. We assume that LVEF is normally distributed (Figures A-1 and A-2). For models 1, 2, and 3, we used a linear regression model for the association of REF and SEF (dependent variables) with each of thirteen cardiac segments (independent variables) with LVEF among the four groups of the patients with ischemia, infarction, artifact or no findings on scans. We used means, and standard deviations in each of the groups. For Model 4, we used logistic regression analysis to determine whether there is a relationship between each of the thirteen segment(s)/ region(s) of ischemia or infarction (dependent variable) and LVEF (REF and SEF) as independent variables. We calculated the p-values of the variables to determine whether there is an association between LVEF and specific segments of the heart with perfusion abnormalities.

Finally, the association between independent variables such as gender, age, FH, prior CAD, and history of cardiac intervention were studied by using multivariable linear regression models.

For analyzing our data, we used STATA. Stata is a general-purpose statistical software with capabilities that include data management, statistical analysis, graphics, simulations, regression analysis (linear and multiple), and custom programming.

RESULTS

Comparisons between each of the thirteen cardiac segments (Figure 2) and their association with REF and SEF among the patients with ischemia, infarction, and artifact were studied. The outcome results adjusted for the patients' age, sex, family history of cardiovascular diseases, documented history of coronary artery disease (CAD), and history of stent placement.

Five hundred and ninety-six patients, including 356 males (56.4%) and 260 females (43.6%) enrolled in our study. The mean age of the patients (Table A-1) was 66 years- old (SD 12, min 30 & Max 99). The mean age (years) of the men was 66.3 (SD 11.4, min 33 & max 99) and the mean age of the women was 65.7 (SD 12.6, min 30 & max 92) (Table A-1). A family history for CVD was positive for 348 (58.2%) patients. Three hundred and sixty-two (60.8%) patients were known to have CAD. By reviewing EHR, 176 (29.6%) patients had a history of stent placement prior to the scans (Table A-2).

According to the findings on MPI, the patients were divided into four groups of ischemia (237 patients), infarction (193 patients), artifact (166 patients) and no findings on scans (69 patients). Left Ventricular Ejection Fraction (LVEF) is also divided into two groups of Rest Ejection Fraction (REF) and Stress Ejection Fraction (SEF). The REF mean for all of the patients was 52.9% (SD 14.2, min10 & max 96), for patients with ischemia 57% (SD 11.8, min 22 & max 96), patients with infarction 47.1% (SD 15.3, min 10 & max 82), patients with artifact 55% (SD 12, min 19 & max 79) and patients with no findings on scan 50.2% (SD 15.1, min 15 & max 80) (Table 2).The SEF mean for all of the patients was 54% (SD 14.2, min12 & max 93), for patients with ischemia 57.4% (SD 11.6, min 28 & max 93), patients with

infarction 47.7% (SD 15, min 12 & max 84), patients with artifact 56.8% (SD 11.9, min 17 & max 80) and patients with no findings on scans scan 53% (SD 16.4, min 12 & max 83) (Table 3).

The association of REF and SEF with each of the thirteen cardiac segments was studied by regression analysis. Coefficient, 95% confidence interval (CI) and p value were calculated (Tables 4 and 5).

The association of each of the thirteen cardiac segments with REF and SEF was also studied by logistic regression analysis. The odds ratio and p value were calculated (Table 6).

Table 1: The table shows the frequency of involvement of each of the thirteen myocardial segments in ischemia, infarction and artifact.

Segment	**Ischemia**	**Infarction**	**Artifact**	**Total**
	N (%)	N (%)	N (%)	N (%)
1	6 (1.7)	2 (0.6)	4 (1.1)	12 (1.2)
2	9 (2.6)	11 (3.3)	4 (1.1)	24 (2.4)
3	12 (3.4)	22 (6.6)	25 (7.1)	59 (5.7)
4	4 (1.2)	2 (0.6)	4 (1.1)	10 (1)
5	17 (4.2)	3 (0.9)	24 (6.8)	44 (4.3)
6	14 (4.1)	17 (5.1)	7 (2)	38 (3.7)
7	21 (6)	37 (11.1)	55 (15.6)	113 (10.9)
8	6 (1.7)	6 (1.8)	23 (6.5)	35 (3.4)
9	17 (4.2)	16 (4.8)	52 (14.7)	85 (8.3)
10	12 (3.4)	11 (3.3)	3 (0.9)	26 (2.6)
11	12 (3.4)	32 (9.6)	54 (15.3)	98 (9.7)
12	5 (1.5)	6 (1.8)	5 (1.4)	16 (1.6)
13	210 (60.9)	169 (50.6)	86 (24.4)	465 (45.1)
Total	345 (100)	334 (100)	353 (100)	1032 (100)

Table 2: Rest Ejection Fraction (REF) shown among four groups of the patients.

REF	Observations	Mean	Std. Dev	Min	25%	50%	75%	Max
Total	596	52.88	14.21	10	45	54	63	96
Ischemia	237	57.00	11.82	22	47	53	60	96
Infarction	193	47.15	15.34	10	30	42	50	82
Artifact	166	55.01	12.00	19	41	50	61	79
No Findings	69	50.23	15.08	15	43	52	61	80

Table 3: Distribution of Stress Ejection Fraction (SEF) among 4 groups of patients

SEF	Observations	Mean	Std. Dev	Min	25%	50%	75%	Max
Total	596	54.03	14.18	12	46	55	64	93
Ischemia	237	57.42	11.58	28	47	54	60	93
Infarction	193	47.66	15.05	12	33	42	50	84
Artifact	166	56.76	11.93	17	42	53	61	80
No Findings	69	53	16.44	12	45	54	63	83

First model: By analyzing the data collected for each patient, REF and SEF were matched and evaluated for any four groups of the scans and association with the segment number involved in perfusion abnormalities. The coefficient, 95% confidence interval (CI) and p value were calculated for each segment for REF and SEF in each of the four groups.

The results were adjusted for age, sex, FH, stent and CAD by calculating multiple linear regression models.

REF: The results show that there was no statistically significant association between decreased REF and the segments in patients with ischemia or artifact.

However, in patients with fixed perfusion defect (infarction), we found a significant association decrease in REF in only some of the segments (segments 9 and 13) (Tables 4 and 5).

SEF: The patients with ischemia show significant association between decreased SEF and the segment 8. The patients with infarction show statistically significant association between decreased SEF and segments 8, 9, 10 and 13. No statistically significant association between decreased SEF and any segments reported as artifact (Tables 4 and 5).

The data show that not all of the cardiac segments experience the same frequency involvement in perfusion abnormalities. Frequency of involvement of each of the thirteen myocardial segments in ischemia, infarction and artifact is shown in Table 1.

Among the infarction group, a significant association was noted with REF for segments 9 and 13 (Figure 2) and with SEF for segments 8, 9, 10 and 13 which is explained in detail here. The decrease in REF among the patients with infarction was shown to be as follows: Segment 9 (distal anterior wall) was associated with a 10.07% decrease with REF (coefficient [-10.07], $p = 0.039$). Segment 13 (apex) was associated with a 4.83% decrease with REF (coefficient [-4.83], $p < 0.0001$). The decrease in SEF among the patients with infarction was the following: Segment 8 (mid septal wall) was associated with a 18.6% decrease with SEF (coefficient [-18.6], $p = 0.011$); Segment 9 (apical anterior wall) was

associated with a 9.93% decrease with SEF (coefficient [-9.93], p = 0.032); Segment 10 (distal lateral wall) was associated with a 11.45% decrease with SEF (coefficient [-11.45], p = 0.035) and Segment 13 (apex) was associated with a 5.48% decrease with SEF (coefficient [-5.48], p < 0.0001). (Tables 4 and 5)

Among the patients with ischemia, we noted that segment 8 (mid septal wall) was associated with a 10.5% decrease with only SEF (coefficient [-10.5], p = 0.038)

Table 4: Association between Rest Ejection Fraction (REF) and 13 cardiac segments among patients with ischemia, infarction or artifact are shown. The results are adjusted for sex, age, FH, CAD and stent.

Segment	Ischemia			Infarction			Artifact		
	Coeff*	95% CI	P Value	Coeff	95% CI	P Value	Coeff	95% CI	P Value
1	5.84	-6.50, 18.20	0.353	-11.69	-30.48, 7.09	0.222	-6.21	-19.44, 7.00	0.356
2	1.39	-12.02, 14.80	0.839	-9.82	-22.95, 3.31	0.142	4.18	-12.07, 20.44	0.613
3	-2.98	-13.65, 0.67	0.582	-5.54	-14.34, 3.25	0.216	1.48	-5.49, 8.46	0.676
4	-5.71	-22.46, 11.02	0.503	-1.51	-26.38, 23.35	0.905	0.92	-12.59, 14.45	0.893
5	6.58	-5.88, 19.06	0.300	-0.261	-17.11, 16.59	0.976	7.12	0.67, 13.56	0.030
6	-2.41	-14.64, 9.82	0.699	3.62	-9.36, 16.61	0.584	-6.02	-18.96, 6.91	0.361
7	8.28	-1.29, 17.86	0.090	3.46	-5.04, 11.98	0.424	-1.60	-7.99, 4.79	0.623
8	-8.59	-24.40, 7.20	0.286	-14.25	-29.24, 0.73	0.062	3.11	-3.66, 9.88	0.367
9	-6.12	-17.61, 5.36	0.296	-10.07	-19.64, -0.51	0.039	-0.87	-6.50, 4.75	0.760
10	-2.49	-12.52, 7.54	0.626	-9.32	-20.53, 1.87	0.103	8.84	-6.74, 24.44	0.266
11	-8.97	-18.86, 0.91	0.075	-4.60	-11.38, 2.17	0.182	2.70	-2.89, 8.30	0.344
12	5.27	-9.58, 20.14	0.486	14.93	0.92, 28.94	0.037	-6.05	-18.26, 6.16	0.331
13	5.49	3.31, 7.67	0.000	-4.83	-7.16, -2.51	0.000	0.52	-2.79, 3.85	0.755

Table 5: Association between Stress Ejection Fraction (SEF) and 13 cardiac segments among patients with ischemia, infarction or artifact are shown. The results are adjusted for sex, age, FH, CAD and stent.

Segment	Ischemia			Infarction			Artifact		
	Coeff*	95% CI	P Value	Coeff	95% CI	P Value	Coeff	95% CI	P Value
1	6.91	-3.10, 16.92	0.176	-14.80	-32.68, 3.077	0.104	-6.03	-18.70, 6.64	0.350
2	1.87	-6.31, 10.05	0.653	-6.36	-18.86, 6.12	0.317	10.81	-4.76, 26.38	0.173
3	-0.43	-7.58, 6.72	0.906	-3.95	-12.32, 4.41	0.353	1.57	-5.12, 8.26	0.645
4	-4.10	-16.36, 8.18	0.513	-0.98	-24.65, 22.67	0.935	3.70	-9.25, 16.66	0.575
5	1.44	-4.56, 7.46	0.636	3.50	-12.52, 19.54	0.668	7.24	1.07, 13.41	0.022
6	0.36	-6.23, 6.96	0.913	5.10	-7.26, 17.46	0.418	-9.15	-21.55, 3.24	0.148
7	1.03	-4.42, 6.49	0.711	1.01	-7.08, 9.11	0.805	-0.10	-6.23, 6.02	0.973
8	-10.5	-20.49, -0.57	0.038	-18.61	-32.87, -4.35	0.011	2.27	-4.22, 8.76	0.493
9	-1.94	-7.93, 4.04	0.524	-9.93	-19.04, -0.833	0.032	-0.46	-5.85, 4.93	0.867
10	0.14	-7.01, 7.29	0.969	-11.45	-22.11, -0.78	0.035	9.84	-5.10, 24.78	0.196
11	-3.05	-10.17, 4.06	0.400	-2.43	-8.88, 4.02	0.460	2.07	-3.29, 7.44	0.447
12	-0.24	-11.26, 10.77	0.965	11.38	-1.94, 24.71	0.094	-8.12	-19.83, 3.57	0.173
13	4.19	2.10, 6.28	0.000	-5.48	-7.69, -3.26	0.000	1.07	-2.11, 4.26	0.510

Second model: To examine the effects of the neighboring segments on REF and SEF, we evaluated if any of the 3 segments of each wall were involved in the perfusion abnormalities (OR). A statistically significant association was seen between the cardiac wall and mean REF and SEF in the following groups of the patients (Tables A-3 and A-4). With this model, we first evaluated if any segments in the cardiac wall were involved in perfusion abnormalities. For example, for the anterior wall, we assessed if Segments 1, 5 or 9 were involved in perfusion abnormalities or not and called it "OR". We also assessed the lateral wall (Segments 2, 6 or 10), inferior wall (Segments 3, 7 or 11) and lateral wall (Segments 4, 8, or 12) in the same manner.

For patients with infarction, the results show that there is a statistically significant association between a decrease in SEF and REF in total if any (OR) segments (2, 6 or 10) of the lateral wall are involved in infarction, which are associated with a 19.29%, 18.30% decrease respectively (coefficient [-19.29], $p < 0.0001$ and coefficient [-18.30], $p < 0.0001$ respectively). In patients with ischemia, there is a statistically significant association between SEF and REF in total if any (OR) segments (3, 7 or 11) of the inferior wall are involved in infarction, which are associated with a 11.95%, 11.80% decrease respectively (coefficient [-11.95], $p < 0.0001$ and coefficient [-11.80], $p < 0.0001$ respectively). Interestingly, we found among the patients with artifact a statistically significant association between SEF and REF and in total if any (OR) segments (2, 6 or 10) of the lateral wall are involved in artifact, which are associated with a 11.26%, 12.81% decrease respectively (coefficient [-11.26], $p < 0.0001$ and coefficient [-12.81], $p < 0.0001$) (Tables A-3 and A-4).

In the third model; we combined all three segments on each cardiac wall together (anterior wall segments 1 and 5 and 9). If all of the segments are involved with perfusion abnormalities, we call it “AND”. We also assessed the lateral wall, inferior wall and septal wall segments using the same method.

The statistically significant association was seen in the patients with ischemia if all of the 3 segments were involved in ischemia together in the inferior wall (coefficient [-11.62], p = 0.007) only with REF. There was no strong association between anterior wall, lateral wall, or septal walls and REF or SEF in patients with ischemia (Tables A-5 and A-6). A statistically significant association was also seen in the patients with infarction if all of the 3 segments were involved in ischemia together in the inferior wall (coefficient [-25.58], p = 0.011) only with SEF.

Tables A-5 and A-6 show insufficient cases when we combined all the segments together (AND) for septal wall among the patients with ischemia, lateral wall among the patients with infarction and septal wall among the patients with artifact. There are no cases with involvement of entire wall segments, on the aforementioned walls.

Fourth model: By analyzing the data collected for each patient, the segment numbers were matched and evaluated for any four groups of the scans and association with decreasing in REF and SEF. The odds ratio (OR) and p-values were calculated for each segment for REF and SEF in each of the four groups. The results were adjusted for age, sex, FH, stent and CAD by calculating multiple linear regression models. The results show that there was no statistically significant association between REF or SEF in the segments in patients with ischemia or artifact. (Table 6)

However, in patients with fixed perfusion defect (infarction), we found a significant association in post-stress EF in only some of the segments (segments 8, 9, 12 and 13) (Tables A-9, A-10, A-11 and A-12). The data didn't show a statistically significant association of SEF if infarction involved other cardiac segments (segments 1, 2, 3, 4, 5, 6, 7, 10, or 11). The Segments 2 and 6 involved in infarction were also statistically significant with REF (Tables A-7 and A-8). There were no other segments with a strong association with REF.

The data shows that not all of the cardiac segments experience the same frequency involvement in perfusion abnormalities. Frequency of involvement of each of the thirteen myocardial segments in ischemia, infarction and artifact is shown in Table 1.

Among the infarction group, a significant association was noted with REF for Segments 2 and 6 (Figure 2), with SEF for Segments 8, 9, 12 and 13 which is explained in detail here. The association between the segments and REF among the patients with infarction was shown to be as follows: Segment 2 (basal lateral wall) shows a significant association with REF (OR 0.86, p = 0.003) and Segment 6 (mid-lateral wall) shows a significant association with REF (OR 0.92, p = 0.034). The association between the segments and SEF among the patients with infarction was the following: Segment 8 (mid septal wall) shows a significant association with SEF (OR 0.71, p = 0.012); Segment 9 (apical anterior wall) shows a significant association with SEF (OR 0.89, p 0.022); Segment 12 (apical septal wall) shows a significant association with SEF (OR 0.83, p = 0.021) and Segment 13 (apex) shows a significant association with SEF (OR 0.96, p = 0.005). (Table 6)

Among the patients with infarction, we noted four segments of myocardium reported in only two cases.

Table 6: The Table shows the association of Rest Ejection Fraction (REF) and Stress Ejection Fraction (SEF) with the myocardial segments. The Odds Ratio and p value were calculated for patients with ischemia, infarction or artifact.

		Ischemia		**Infarction**		**Artifact**	
Segment	LVEF	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value
1	REF	1.06	0.408	1.17	0.431	.95	0.568
	SEF	1.00	0.972	.74	0.230	1.02	0.825
2	REF	.99	0.803	.86	0.003	.89	0.254
	SEF	1.03	0.639	1.10	0.061	1.18	0.169
3	REF	1.07	0.142	.95	0.146	.98	0.662
	SEF	.93	0.173	1.02	0.669	1.04	0.318
4	REF	.86	0.098	Insufficient data Total 2 cases		.92	0.352
	SEF	1.12	0.193			1.15	0.230
5	REF	1.03	0.508	.82	0.157	1.02	0.601
	SEF	.99	0.762	1.09	0.445	1.04	0.230
6	REF	.98	0.634	.92	0.034	.99	0.942
	SEF	1.03	0.592	1.04	0.306	.98	0.763
7	REF	1.07	0.069	.97	0.362	.97	0.285
	SEF	.95	0.166	.99	0.710	1.04	0.132
8	REF	1.02	0.726	1.23	0.055	1.03	0.407
	SEF	.91	0.206	.71	0.012	.99	0.721
9	REF	1.03	0.469	1.02	0.591	1.01	0.759
	SEF	.96	0.356	.89	0.022	1.01	0.706
10	REF	.95	0.318	.98	0.705	.95	0.632
	SEF	1.06	0.289	.97	0.554	1.12	0.347
11	REF	1.03	0.513	.95	0.100	.99	0.756
	SEF	.95	0.307	1.01	0.820	1.03	0.196
12	REF	1.01	0.947	1.17	0.050	1.02	0.786
	SEF	1.00	0.973	.83	0.021	.95	0.433
13	REF	1.04	0.005	1.00	0.828	.99	0.614
	SEF	.99	0.712	.96	0.005	1.02	0.307

DISCUSSION

This study demonstrates that in patients with myocardial infarction, some of the cardiac segments have a significant association with REF and SEF.

Our hypothesis was that the LVEF will be most reduced when perfusion abnormalities involve anterior wall segment(s)/region(s), compared with the damage to the other myocardial segments/region(s).

It has been demonstrated that global left ventricular function is significantly more affected after anterior MI in patients with reversible ischemia in addition to fixed wall defects. [47]. The relationships between infarct size with LV ejection fraction (EF) and volumes were examined in 215 myocardial infarction patients [42].

Our study endpoint was to identify which segment/region of the myocardium, when damaged following myocardial perfusion abnormalities such as ischemia or infarction, has the maximum negative effect on LVEF and to gain an understanding of the association of LVEF with regional ischemia/ infarction which helps to improve or prevent heart failure. Several studies have shown a significant association between revascularization and improved survival rate in patients with LV dysfunction and evidence of myocardial viability independently of the imaging technique used. [44].

The prognostic value of stress SPECT perfusion imaging has been established in earlier clinical studies [25, 26]. The major prognostic regional LV variables predictive of future hard cardiac events are large defect size (> 20% of LV), defects in more than one coronary vascular territory indicating multi-vessel disease, reversible defect in multiple myocardial segments, and numerous nonreversible defects [27]. Our results indicate that

there are more localized perfusion abnormalities after myocardial infarction and ischemia, which could be important for treatment and prognosis [25–27].

In this study, global LV (REF and SEF) function did not show a strong association between the segments/ locations in patients with artifact (Models1, 3 and 4). However, the artifact group showed a significant association between global REF and SEF parameters when more than one segment is reported on the lateral wall (Model 2), which may require more investigation. The group of patients with infarction showed an association between decreased REF/SEF and regional/segmental perfusion abnormality. A comparable decrease in REF is seen when infarction involved Segments 9 and 13. There was a significant decrease in SEF when infarction involved the mid septal wall, apical anterior wall, apical lateral wall and apex (Segments 8, 9, 10 and 13). When any of or combination of the three segments are involved in infarction, the lateral wall showed a significant decrease in REF and SEF (Model 2 “OR”), although, when the entire cardiac walls (Model 3 “AND”) are involved in infarction, there was no significant decrease in REF and SEF. The patients with ischemia showed a statistically significant decrease in SEF when Segment 8 was involved in the perfusion abnormality. These ischemia patients also had a significant decrease in REF and SEF when the inferior wall is involved with more than one segment (Model 2). If ischemia involved the entire wall, the inferior wall showed an association with a decrease in REF (Model3).

In contrast, we used gated SPECT Myoview with the post-stress imaging delay of approximately 30 minutes, which limited our ability to evaluate LV function immediately after stress. Subgroup analyses of patients with or without perfusion defect revealed an

approximate 1–3% increase in post- stress EF when compared to REF in all four groups of the patients with ischemia, infarction, artifact or no findings on scans (Tables 3 and 4).

We created four models for assessment of the individual segments and or combination of the segments of the cardiac walls and LVEF (see below).

The first model: It was designed for the evaluation of REF and SEF with each of the 13 segments individually in the groups of patients with ischemia, infarction, and artifact. In the group with infarction, the anterior-apical and apex segments (9 & 13) showed an association with decrease REF 10.07% and 4.83% respectively (coefficient [-10.07], [-4.83] respectively). This group also showed significant association with decrease SEF 18.61%, 9.93%, 11.45% and 5.48% respectively when the segments 8, 9, 10 and 13 are involved (coefficient [-18.61], [-9.93], [-11.45], [-5.48] respectively). The prognoses after interventions, rehabilitation or follow up should be studied for this group. We also found in the first model that the mid septal wall segment (8) showed strong association with only decease SEF 10.5% in patients with ischemia (coefficient [-10.5]). The strongest association between LVEF and segmental abnormalities is seen with mid septal wall segment (8) post infarction with a decrease of 18.61% with SEF (coefficient [-18.61]). These findings may show that the patients with infarction are suffering the most from decreased LVEF and this group may receive more benefit from reperfusion therapies to prevent heart failure. A study could be designed to compare this group of patients with or without interventions and to assess the outcome.

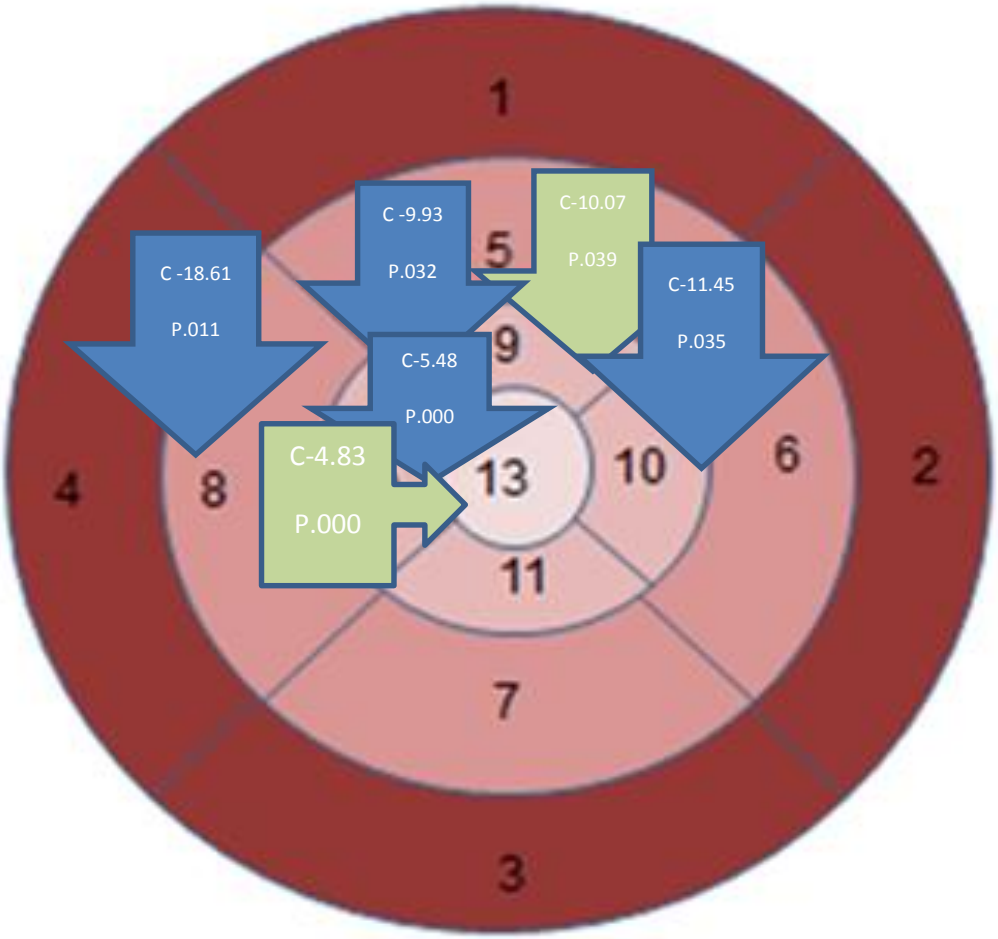

Figure 3: Association of Rest Ejection Fraction (REF, green arrows) and Stress Ejection Fraction (SEF, blue arrows) with segmental infarction. Coefficient (C) and p values are shown. No statistically significant association with REF and SEF with artifact is identified. The results are adjusted for age, sex, FH, CAD and stent.

Second model: When we combined the neighboring segments (second model) in a group of patients with infarction and artifact, we found a statistically significant association between lateral wall segments with decrease REF 18.30% and 12.81% respectively (coefficient [-18.30] and [-12.81] respectively) and decrease SEF 19.29% and 11.26% respectively (coefficient [-19.29] and [-11.26] respectively). The patients with ischemia also

showed a significant association with decreased 11.80% and 11.95% with REF and SEF in the inferior wall respectively (coefficient [-11.80] and [-11.95] respectively). This may represent the effect of the infarction size when it gets bigger and extends to neighboring segments could decrease REF or SEF significantly.

Model Three: When we only studied patients who had entire wall involvement with perfusion abnormalities, we found strong association between the inferior wall and decrease REF 11.62% in patients with ischemia (coefficient [-11.62]). We also found a strong association between the inferior wall and decrease SEF 25.58% in patients with infarction (coefficient [-25.58]). We were not able to evaluate all three of the cardiac walls in patients with ischemia, infarction and artifact due to insufficiencies of the data [Tables A-5 and A-6].

As seen in Tables A-5 and A-6, by combining all 3 of the segments on each wall, we found that there were not enough cases which had involvement of the whole cardiac wall with the perfusion abnormalities. Due to this data insufficiency, analyzing the data was not possible for that wall with perfusion abnormalities. This data insufficiency was only seen if we combined all 3 of the segments together (AND).

Model Four: In this model we studied the association between each of 13 cardiac segments (dependent variables) and REF/ SEF as independent variables. The result shows that no association between any of the thirteen segments with REF and SEF in patients with ischemia and infarction. There is association with Segments 2 and 6 with REF. This showed the odds of infarction at Segments 2 and 6 decreases 0.86 and 0.92 respectively, with each percentage point increase of REF when adjusted for variables, age, sex, CAD and FH.

There is association with Segments 8, 9, 12 and 13 with SEF. This showed the odds of infarction at Segments 8, 9, 12 and 13 decreases 0.71, 0.89, 0.83 and 0.96 respectively with each percentage point increase of SEF when adjusted for variables, age, sex, CAD and FH (Figure 4).

Our findings of the stronger association between some cardiac segments rather than others with REF and SEF in patients with coronary arteries perfusion abnormalities generate new questions for future investigation regarding LVEF and regional perfusion abnormalities. Using gated SPECT 201Tl, Itti et al. [28] suggested that the decrease in SEF depends on the reversibility of the perfusion defect since patients with ischemia show more impaired contractility. They also found that, because of an imbalance between myocardial needs and supplies, perfusion changes are first seen followed by degradation of contraction. Our study did not find a significant association between REF and individual segmental ischemia. However, this association was found in SEF with only Segment 8 involved. The inferior wall showed a significant decrease in REF and SEF with more than one segment involved or with REF if the entire inferior wall is involved in ischemia. Further study should examine the association of the septal walls when the entire wall is involved in ischemia. Prognostic further study should also examine the association of the lateral wall when the entire wall is involved in infarction.

Our hypothesis is rejected by the results since we found that “LVEF won’t be reduced most when perfusion abnormalities involve anterior wall segment(s)/region(s), compared with damage to the other myocardial segments/region(s)”. The only segment of the anterior wall that showed strong association with REF and SEF was the anterior apical

segment (Segment 9). The septal wall showed a stronger association with SEF with Segment 8 and the lateral wall also showed a strong association with SEF with Segment 10. Apex also shows a strong association with both REF and SEF (Figure 3).

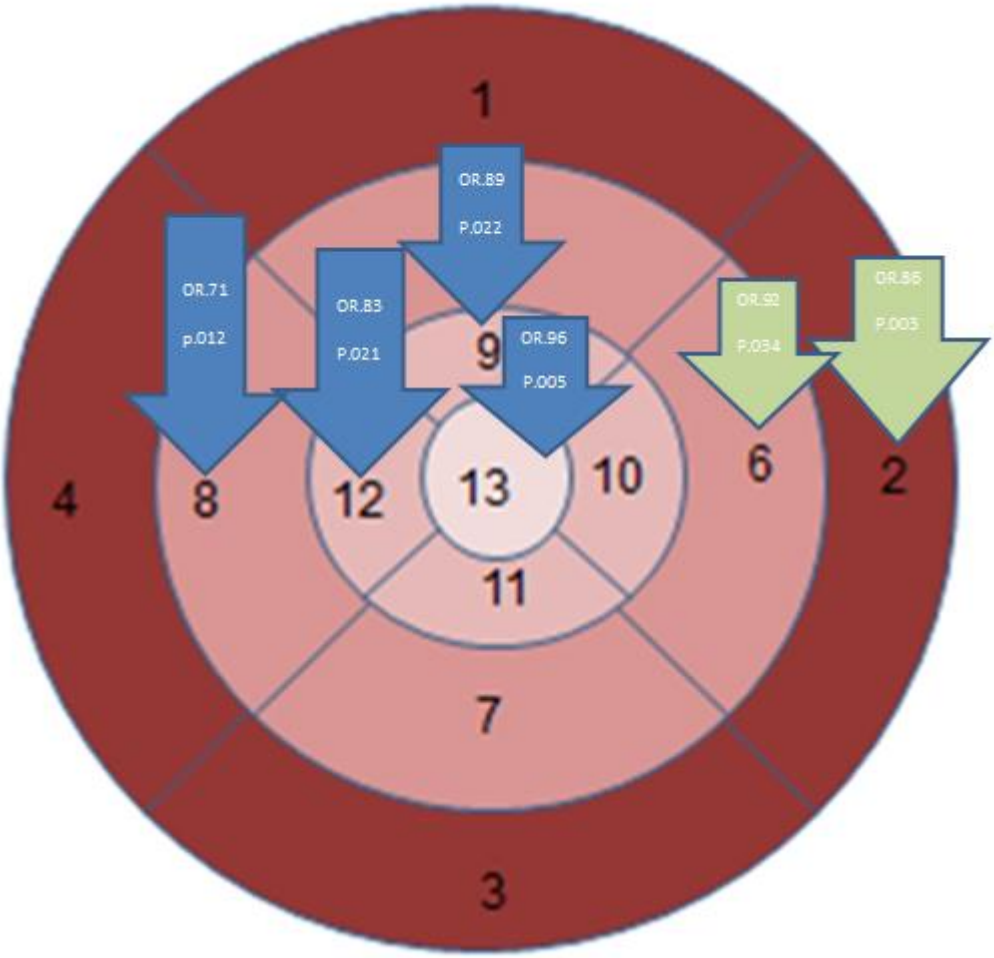

Figure 4: Association of segmental infarction with Rest Ejection Fraction (REF, green arrows) and Stress Ejection Fraction (SEF, blue arrows). Odds ratios and p values are shown. No statistically significant association with REF and SEF with ischemia and artifact are identified. The results are adjusted for age, sex, FH, CAD and stent.

These results may help to prevent heart failure secondary to myocardial perfusion abnormalities. Left ventricular disease precedes the onset of symptoms of cardiac dysfunction. Identification of early cardiac disease could allow intervention that may be effective in slowing progression. By knowing in which cardiac segment(s) a perfusion abnormality drops LVEF the most, appropriate investigation and intervention can be prioritized to restore myocardial perfusion for the segment(s) to prevent HF.

Our study has some limitations. With respect to the segments/locations of perfusion abnormalities, we did not evaluate the impact of the severity of perfusion abnormalities and the effect of these perfusion abnormalities on cardiac wall motion. Our patients' population may be different with other patients' population based the geographic location as a result of racial distribution differences. Our patient sample was relatively small (596 subjects), which resulted in insufficient data when we studied the entire wall perfusion abnormalities. This caused a limitation of the interpretation. Each scan was visually assessed for perfusion abnormalities by two nuclear medicine physicians.

We also wish to point out that increasingly PET-based cardiovascular imaging will play a major role in this important healthcare domain. PET provides substantially higher quality images compared to those generated by SPECT. The spatial resolution of PET is quite optimal for detecting subtle abnormalities that frequently cause significant dysfunction in cardiac disorders. Combined cardiac and respiratory gating is only feasible by PET and almost impossible with SPECT. This additional technical step further improves image quality, and therefore, its effectiveness in identifying subtle abnormalities. Also, a rapidly evolving list of PET radiotracers available for assessing both myocardial perfusion and

molecular/cellular disorders in the cardiovascular system makes PET a unique imaging modality in the future. Therefore, we believe by employing this technology, we will be able to investigate the underlying molecular and cellular abnormalities that lead to cardiac dysfunction and asses the effectiveness of existing and future therapeutic interventions.

CONCLUSION

Gated SPECT Myoview in patients with myocardial infarction shows strong association with multiple cardiac segments either with Stress Ejection Fraction (SEF) (Segments 8, 9, 10, and 13) or with Rest Ejection Fraction (REF) (Segments 9 and 13) in the patients with infarction. This association wasn't seen in patients with artifact. In the group of patients with ischemia, association was only seen with SEF and Segment 8. A decrease in global LVEF depends on the location of perfusion abnormalities. Some cardiac segments show a greater association with decreased REF and SEF. This early detection allows heart failure to be treated early in its course and guides the management of patients for an appropriate therapy to reduce the negative impact of symptomatic diseases, such as disability or death.

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APPENDIX A: DATA TABLES AND FIGURES

Tables

Table A-1: Distribution of Age.

Age	subjects	Mean	Std. Dev	Min	Max
Total	596	66.04	11.97	30	99
Female	260	65.66	12.65	30	92
Male	336	66.33	11.43	33	99

Table A-2: Distribution of FH, DM, CAD, stent and CABAG.

	Family History for CVD	Known CAD	Stent
Positive	348 (58.2%)	362 (60.8%)	176 (29.6%)
Negative	234 (39.3%)	234 (39.2%)	420 (70.4%)
Unknown	14 (2.5%)		

Table A-3: Association between Rest Ejection Fraction (REF) and if more than one cardiac segments (OR) involved in each cardiac wall among patients with ischemia, infarction or artifact are shown. The results are adjusted for sex, age, FH, CAD and stent.

Location	LVEF	Ischemia			Infarction			Artifact		
		Coeff *	95% CI	P Value	Coeff	95% CI	P Value	Coeff	95% CI	P Value
Anterior Wall	REF	1.85	-4.16, 7.86	0.545	-2.16	-8.54, 4.22	0.506	-0.34	-5.96, 5.27	0.905
Lateral Wall	REF	-5.96	-15.46, 3.52	0.218	-18.30	-26.42. -10.19	0.000	-12.81	-19.06, -6.55	0.000
Inferior Wall	REF	-11.80	-16.08, -7.52	0.000	0.32	-10.74, 11.37	0.955	5.85	1.28, 10.43	0.012
Septal Wall	REF	-1.27	-9.98, 7.44	0.774	-1.07	-4.56, 2.41	0.546	-2.37	-8.61, 3.85	0.454

Table A-4: Association between Stress Ejection Fraction (SEF) and if more than one cardiac segments (OR) involved in each cardiac wall among patients with ischemia, infarction or artifact are shown. The results are adjusted for sex, age, FH, CAD and stent.

Location	Ischemia			Infarction			Artifact		
	Coeff*	95% CI	P Value	Coeff	95% CI	P Value	Coeff	95% CI	P Value
Anterior Wall	0.49	-5.50, 6.49	0.871	-2.37	-8.68, 3.93	0.460	-3.02	-8.64, 2.59	0.291
Lateral Wall	-5.52	-14.99, 3.94	0.252	-19.29	-27.31, -11.27	0.000	-11.26	-17.52, -5.01	0.000
Inferior Wall	-11.95	-16.22, -7.68	0.000	-4.87	-15.81, 6.05	0.381	5.92	1.35, 10.49	0.011
Septal Wall	-0.61	-9.30, 0.07	0.889	-0.55	-4.00, 2.89	0.752	-2.73	-8.96, 3.49	0.389

Table A-5: Association between Rest Ejection Fraction (REF) and if all three cardiac segments (AND) involved in each cardiac wall among patients with ischemia, infarction or artifact are shown. The results are adjusted for sex, age, FH, CAD and stent.

Location	Ischemia			Infarction			Artifact		
	Coeff*	95% CI	P Value	Coeff	95% CI	P Value	Coeff	95% CI	P Value
Anterior Wall	7.92	-19.88, 35.72	0.576	-3.25	-17.24, 10.74	0.648	0.43	-15.73, 16.58	0.958
Lateral Wall	-2.08	-29.88, 25.72	0.883	Insufficient data, total 0 cases			-9.56	-25.72, 6.58	0.245
Inferior Wall	-11.62	-20.08, -3.17	0.007	-16.50	-36.25, 3.25	0.101	6.09	-13.67, 25.87	0.545
Septal Wall	Insufficient data, total 0 cases			-1.55	-8.23, 5.12	0.647	Insufficient data, total 0 cases		

Table A-6: Association between Stress Ejection Fraction (SEF) and if all three cardiac segments (AND) involved in each cardiac wall among patients with ischemia, infarction or artifact are shown. The results are adjusted for sex, age, FH, CAD and stent.

Location	Ischemia			Infarction			Artifact		
	Coeff*	95% CI	P Value	Coeff	95% CI	P Value	Coeff	95% CI	P Value
Anterior Wall	1.86	-25.99, 29.71	0.896	-1.58	-15.49, 12.33	0.824	-4.35	-20.48, 11.76	0.596
Lateral Wall	1.85	-26.00, 29.70	0.896	Insufficient data, total 0 cases			-5.02	-21.15, 11.10	0.541
Inferior Wall	-7.41	-15.88, 1.05	0.086	-25.58	-45.23, -5.92	0.011	9.47	-10.25, 29.20	0.346
Septal Wall	Insufficient data, total 0 cases			0.86	-5.77, 7.50	0.798	Insufficient data, total 0 cases		

Table A-7: Regression model for association between infarction at Segment 2 with other variables.

Infarct2	Odds Ratio	Std. Err.	z	P>z	[95% Conf. Interval]	
Sex	.99	.69	-0.01	0.992	.25	3.91
age	1.03	.03	0.93	0.350	.96	1.09
FH	1.53	.91	0.72	0.475	.47	4.89
CAD	2.01	1.91	0.73	0.463	.31	13.02
stent	1.26	.92	0.32	0.750	.30	5.30
REF	.86	.04	-2.94	0.003	.78	.95
SEF	1.10	.05	1.87	0.061	.99	1.21

Table A-8: Regression model for association between infarction at Segment 6 with other variables.

Infarct6	Odds Ratio	Std. Err.	z	P>z	[95% Conf. Interval]	
Sex	1.32	.73	0.51	0.612	.45	3.92
age	1.03	.02	1.26	0.208	.98	1.08
FH	1.38	.66	0.69	0.490	.54	3.51
CAD	3.86	3.24	1.61	0.108	.74	20.03
stent	.87	.49	-0.25	0.805	.28	2.63
REF	.91	.04	-2.12	0.034	.84	.99
SEF	1.04	.04	1.02	0.306	.96	1.13

Table A-9: Regression model for association between infarction at Segment 8 with other variables.

Infarct8	Odds Ratio	Std. Err.	z	P>z	[95% Conf. Interval]	
Sex	7.58	8.12	1.89	0.058	.93	61.73
age	.96	.04	-0.91	0.363	.87	1.04
FH	1.22	1.41	0.18	0.859	.13	11.64
CAD	.02	0.01	-9.93	0.000	.01	.04
stent	1.27	1.48	0.21	0.836	.13	12.49
REF	1.23	.13	1.92	0.055	.99	1.53
SEF	.71	.09	-2.53	0.012	.54	.92

Table A-10: Regression model for association between infarction at Segment 9 with other variables.

Infarct9	Odds Ratio	Std. Err.	z	P>z	[95% Conf. Interval]	
Sex	.84	.52	-0.28	0.781	.24	2.88
age	.97	.02	-0.84	0.398	.93	1.02
FH	.87	.45	-0.26	0.791	.31	2.43
CAD	1.75	1.58	0.62	0.536	.29	10.29
stent	1.22	.76	0.33	0.742	.36	4.18
REF	1.02	.04	0.54	0.591	.94	1.12
SEF	.89	.043	-2.29	0.022	.81	.98

Table A-11: Regression model for association between infarction at Segment 12 with other variables.

Infarct12	Odds Ratio	Std. Err.	z	P>z	[95% Conf. Interval]	
Sex	1.51	1.48	0.42	0.674	.22	10.33
age	.97	.040	-0.63	0.528	.89	1.05
FH	.26	.24	-1.43	0.152	.04	1.63
CAD	.012	.01	-9.93	0.000	.01	.04
stent	1.51	1.42	0.44	0.661	.24	9.51
REF	1.16	.09	1.96	0.050	.99	1.36
SEF	.83	.06	-2.31	0.021	.71	.97

Table A-12: Regression model for association between infarction at Segment 13 with other variables.

Infarct13	Odds Ratio	Std. Err.	z	P>z	[95% Conf. Interval]	
Sex	1.30	.27	1.24	0.215	.85	1.97
age	1.01	.01	1.36	0.174	.99	1.03
FH	.94	.17	-0.30	0.764	.66	1.35
CAD	1.42	.36	1.37	0.171	.86	2.34
stent	1.18	.27	0.72	0.470	.75	1.87
REF	1.00	.01	0.22	0.828	.97	1.03
SEF	.95	.015	-2.80	0.005	.93	.98

Figures

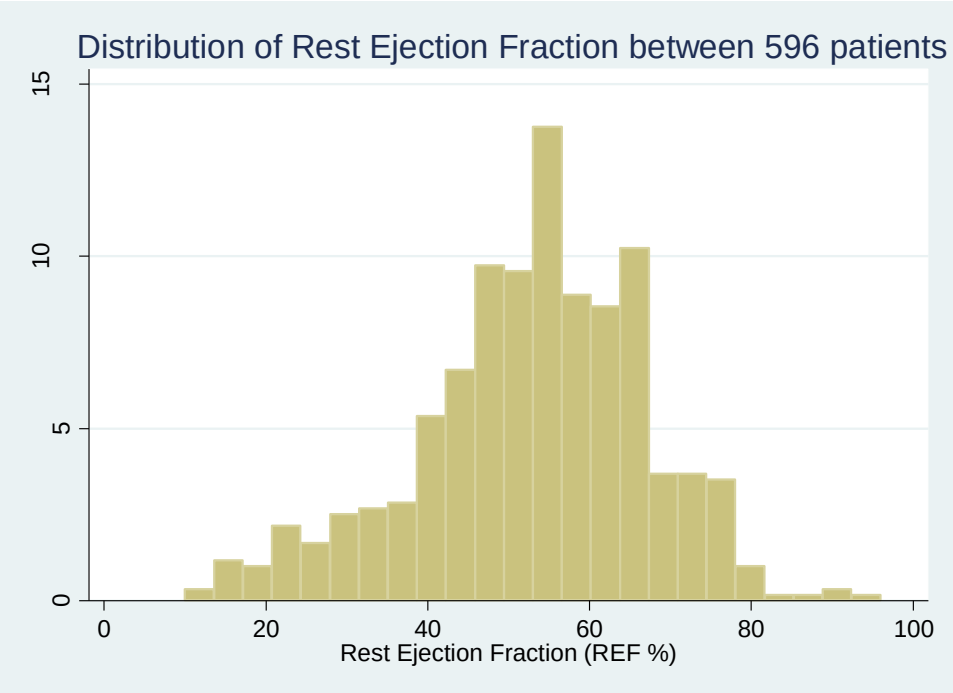

Figure A-1: Distribution of Rest Ejection Fraction among all patients.

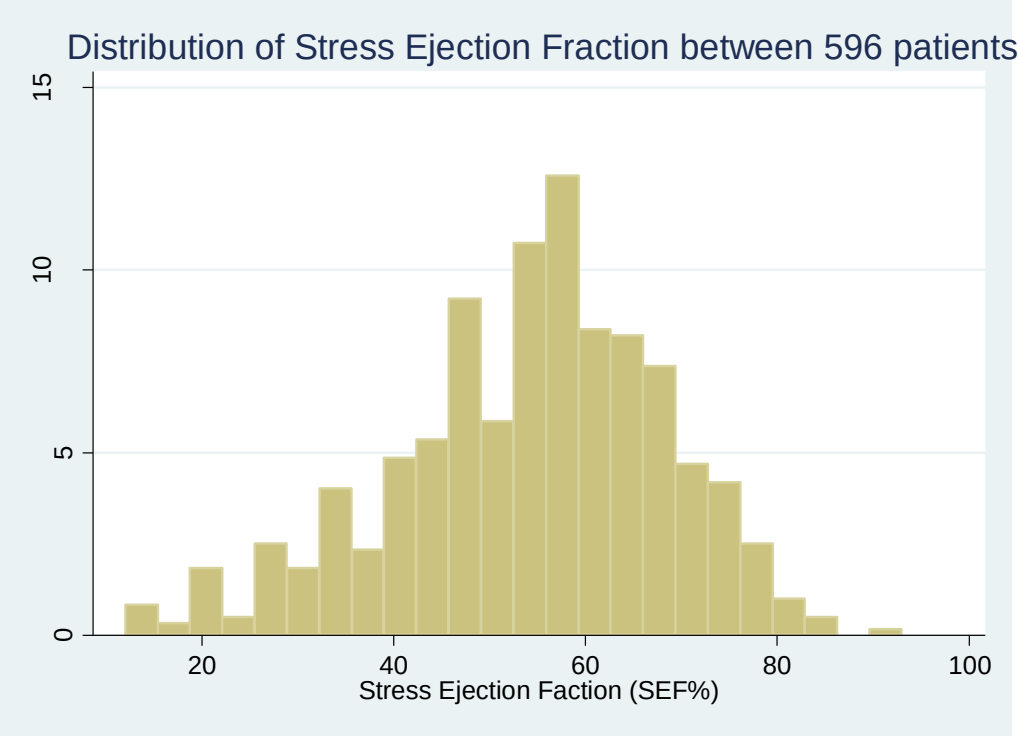

Figure A-2: Distribution of Stress Ejection Fraction among all patients.