"Use of two dimensional echocardiography Speckle Tracking Echocardiography for quantitative assessment of global left ventricular function in comparison to two dimensional Ejection Fraction and three dimensional Ejection Fraction"

A dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY, CHENNAI

In partial fulfillment of

DM - Branch II CARDIOLOGY

Examination to be held in February 2015

C E R T I F I C A T E

This is to certify that the dissertation entitled

"Use of Two-Dimensional Speckle-Tracking Echocardiography for Quantitative Assessment of Global Left Ventricular Function in comparison to 2 D ejection fraction and 3 D ejection fraction"is a bonafide work done by

PARVEEN KUMAR

Christian Medical College, Vellore, Tamil Nadu

in partial fulfillment of the University rules and regulations for award of

DM - Branch II CARDIOLOGY

under my guidance and supervision during the academic year 2011-14

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Last but not the least, I thank to all the patients who agreed to be a part of this study and rendered their co-operation.

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A sum of 5,000/- INR (Rupees Five Thousand only) will be granted for 2 months.

Yours Sincerely

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October 16, 2014

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Sub: **Fluid Research grant project:**
Use of Two-Dimensional Speckle-Tracking Echocardiography for Quantitative Assessment of Global Left Ventricular Function in comparison to 2 D ejection fraction and 3 D ejection fraction.
Dr. Parveen Kumar, Tutor, Cardiology, Dr. Jacob Jose, Cardiology, CMC, Vellore.

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Dear Dr. Parveen Kumar,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

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

With best wishes,

Dr. Nihal Thomas
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ABSTRUCT

Title of study:

Use of Two-Dimensional Speckle-Tracking Echocardiography for Quantitative Assessment of Global Left Ventricular Function in comparison to 2 D ejection fraction and 3 D ejection fraction

Objective:

1.To determine whether global strain derived from 2 D speckle tracking echocardiography (STE) are as accurate as three dimensional (3D) ejection fraction and two dimensional left ventricular (LV) ejection fraction.

2.To see intra-observer and inter-observer variation in measuring 2D global strain and 2 D ejection fraction and 3 D ejection fraction.

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ABSTRACT

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Use of Two-Dimensional Speckle-Tracking Echocardiography for Quantitative Assessment of Global Left Ventricular Function in comparison to 2 D ejection fraction and 3 D ejection fraction

Objective:

1.To determine whether global strain derived from 2 D speckle tracking echocardiography(STE) are as accurate as three dimensional (3D) ejection fraction and two dimensional left ventricular (LV) ejection fraction.

2.To see intra-observer and inter-observer variation in measuring 2D global strain and 2 D ejection fraction and 3 D ejection fraction.

Methods:

This prospective observational study was planned to include 100 patients with LV systolic dysfunction (defined as patient with EF less than 50%) from cardiology inpatient and outpatient. All the patients underwent detailed Echocardiography with 2D speckle tracking and 3D echocardiography. Baseline characteristics of patients were noted. The aim of study was to determine whether global strain derived from 2 D speckle tracking echocardiography (STE) is as accurate as three dimensional (3D) ejection fraction and two dimensional ejection fraction.

Results:

This study showed that there is strong co-relation between speckle tracking echocardiography derived 2D global strain and LV ejection fraction. Although both global longitudinal strain (GLS) and global circumferential strain (GCS) has co-related well with LV function assessment using 2D and 3D echocardiography, but GLS has better co-relation than GCS in our study. This study also showed low inter-observer and intra-observer variability in calculating 2D STE derived global strains and 3D ejection fraction.

Conclusion:

This study has proved that the feasibility and accuracy of 2D speckle tracking echocardiography assessment in a wide range of LV function. This study population also enabled us to understand that these results can be generalised and can be applied in real life clinical practice. The strong reproducibility as shown by low intra-observer and inter-observer variability makes 2D STE derived global strains a robust marker with potential clinical use.

INTRODUCTION

2 D echocardiography is widely used in clinical practice to assess left ventricular function and its importance is recognized by various guidelines. Among proposed validated parameters, the EF is recognized as an important criterion for heart failure prognosis(1) and for pharmacologic, defibrillator and resynchronization therapies (2).A strong relationship between the LV EF and mortality was established in patients with heart failure (3).

However, EF quantification requires the manual endocardial tracking of end diastolic and end systolic frames from 2D imaging, is time consuming and is restricted by a high level of measurement variability. The need for formal quantitative assessment of myocardial systolic function remains a significant challenge.

Recently, new technologies based on deformation measurements have been shown to identify early myocardial dysfunction before EF decrease. Consequently, tools such as 2D strain have been incorporated into echocardiography systems allowing for fast, reliable and reproducible calculation of longitudinal components of LV systolic dysfunction.

As per the guidelines by the American college of cardiology foundation and American heart association, LV systolic dysfunction is defined as patient with ejection fraction less than 50% (4).Global strain measurements by 2D STE have excellent correlations with LVEF validated by both three dimensional echocardiography and cardiac magnetic resonance imaging(5) .Global strain derived by 2 D STE may be superior to LV EF by echocardiography as a powerful prognostic predictor of cardiac events in patients with heart failure (6). Recently three dimensional STE derived global strain has also gaining same importance as 2D STE derived global strains(7).

In our study, we Included 100 patients having LV systolic dysfunction of varied etiology. Patients were taken from cardiology inpatient and outpatient. This study was planned to see whether global strain derived by 2 D speckle tracking is as accurate as 3D EF and 2D EF for assessment of LV ejection fraction

AIMS AND OBJECTIVES

PRIMARY AIM:

To determine whether global strain derived from 2 D speckle tracking echocardiography(STE) are as accurate as three dimensional (3D) ejection fraction and two dimensional ejection fraction for assessment of left ventricular function.

SECONDARY AIM:

To see intra-observer and inter-observer variation in measuring 2 D STE derived global strains and 3 D ejection fraction.

REVIEW OF LITRETURE

Two dimensional (2D) echocardiography is routinely used in clinical practice to assess left ventricular function. Value of 2D echocardiography has been validated by various guidelines also. It is ideally well suited for cardiac mechanics because of its dynamic nature. Echocardiography has long been the main tool for assessment of dynamic cardiac mechanics for decades. But in last decade new automated techniques are being developed for analysis of cardiac function are being developed by manufacturers and researchers of ultrasound technology.

Lot of techniques have come into picture over past decades to address the issue of inter-measurement variability and reader's experience. Some of them have become part of routine practice and others remain limited to research arena. Out of these, two techniques have become the part of routine clinical practice from research arena: (1) Doppler based tissue velocity measurement and (2) speckle tracking derived measurements of strain and stress. Both of these measurements lead to multiple parameters of left ventricular myocardial function.

Terms and definitions(8)**:**

Displacement: is defined as the distance of certain feature like speckle or myocardial fibre moved between two consecutive frames. It is measured in centimetres (cm).

Strain: It is fractional change in length of myocardial fibres. It indirectly indicates myocardial deformation .Strain can have positive or negative value which directly reflects lengthening or shortening respectively. In simple terms, if 20cm string stretched to 25cm, then strain would be 25%. It is a unit less value.

Strain rate: It is defined as rate of change in strain and expressed as 1/sec.

Velocity: It is defined as displacement per unit of time and is measured in cm per seconds.

Velocity and displacement are vectors. So, in addition to magnitude they have direction also. So, these have spatial components along x, y and z directions. These directions can be in the form of radial, longitudinal or circumferential for myocardial mechanics. Similar reason applies to strain and strain rate. Most important advantages of strain and strain rate is that strain or strain rate reflect regional function independent of translational motion.

“Principal strain” defines the local direction and magnitude of lengthening or shortening of myocardium.”Global strain” refers to the average strain in the entire myocardium which is calculated by averaged segmental strain in each myocardial wall segment. Global strain can be in the form of longitudinal, circumferential, radial or area strain.

Two dimensional (2D) speckle tracking Echocardiography (STE):

STE is relatively new and angle independent technique for assessment of myocardial function. The speckle seen in gray scale B-mode images are the result of constructive and destructive interference of ultrasound backscattered from structures smaller than the ultrasound wavelength .By this technology, random noise is filtered out, while keeping small temporarily stable and unique myocardial features referred to as speckles(9).

Kernels or blocks of speckles can be tracked from frame to frame using block matching and provide local displacement information, from which parameters of myocardial function such as velocity, strain and strain rate can be derived. In addition to, instantaneous velocity vectors can be calculated and superimposed on dynamic images.

In contrast to Tissue Doppler imaging (TDI), analysis of these velocity vectors allows quantification of strain and strain rate in any direction(10). STE already been validated for assessment of myocardial deformation in comparison to sonomicrometry(11) and clinically against TDI(12).

Image acquisition: STE can be done in offline mode using earlier acquired 2 D images. Using low frame rates for acquisition of images may result in loss of speckles because in successive frames it may move out of plane or desired area. On the contrary, high frame rate my result into reduction in spatial resolution and quality of image(13). Therefore, high frame rates should be used to avoid under sampling in patients with increased heart rate.

Focus should be positioned to optimize the image quality and depth and width to be adjusted according to area of interest. Data sampling should start >100msec before peak of R wave of first QRS complex and 200msec after last

QRS to allow correct identification of QRS complex otherwise it may lead to erroneous calculation. Apical foreshortening should be minimized because it may affect 2D STE results. Short axis of left ventricle should be made as circular shaped to correct radial and circumferential strain(8).

2D STE analysis: It measures the above 4 parameters by tracking the intra-myocardial speckles or myocardial deformation in imaging plane. These parameters have already been validated in comparison to cardiac MRI(13).

2D strain by using STE is a semiautomatic analysis which requires manual delineation of endocardial borders and subsequent acquisition by machine using automated software .Subsequently, the area of interest to be adjusted accordingly to make most of wall thickness and avoiding pericardium. Aortic valve opening is defined by peak of R wave and aortic valve closure by end of T wave.

Suboptimal tracking is a potential problem in estimation of 2D STE strain. Another limitation is its oversensitivity to pick up reverberations and acoustic shadowing which may lead to underestimation of true deformation.

Advantages and disadvantages of 2D STE:

STE has an advantage of measuring 2D strain in any direction of myocardial motion within the imaging plane, whereas TDI acquired imaging can measure strain only along the direction of ultrasound beam. So, we can measure circumferential or radial strain in same imaging plane. But, 2D STE is also not completely angle independent because echo images have better resolution when the ultrasound probe is parallel as compared to perpendicular direction.

As in other echo measurements, it also depends upon good image quality. 2D STE technique has limited reproducibility when image quality is poor. It also depends upon the assumption that morphological details tracked in one frame to next frame, but actually it may be happening out of plane. So, myocardial deformation is affected by loss of speckles when motion is occurring out of plane(14).

Because STE relies on high temporal resolution, TDI may be advantageous while evaluating patients with fast heart rate e.g. stress echocardiography(8).

A significant limitation of 2D STE is differences among vendors because data analysis is done in polar format which cannot be analysed by other vendor format. There is limited experience to compare inter-vendor variability(15).

Global longitudinal strain by 2D STE has already been validated by cardiac magnetic resonance imaging in various studies to be an effective method of LV function quantification(5).

Three Dimensional Speckle Tracking Echocardiography:

In comparison to 2D STE, 3D STE can track the motion of speckle in any direction as long as they stay in selected scan volume .3D STE much more reliable than 2 D STE in calculating LV volume as shown in MRI(magnetic resonance imaging) based studies(16).

Advantages:

3D STE allows accurate assessment of ventricular dynamics.

1) It can add third component of motion vector which is not visible to 2D STE or TDI. It can overcome the geometric assumptions of 2D speckle tracking echocardiography.

2) It can acquire entire left ventricle in a single volume data set which can calculate all 17 segments strains.
3) It can calculate all four types of strain (longitudinal, circumferential, radial and area strain) in a single.
4) Time from image acquisition to postdata processing analysis is much lesser than two dimensional speckle tracking echocardiography.

Disadvantages:

1) Major limitation of 3D STE is image quality which strongly affects accuracy of strain measurements. In general, 3D data stes are comprised of multiple sectors and stitching noise may be caused around the borders between sectors. Relatively low resolution and random noise affects its ability to define epicardial and endocardial boundaries. So, tracking should be carefully verified and adjusted accordingly.

2) In atrial fibrillation multibeat system is not available. However, recent advanced systems with a single beat might overcome the limitations. But, it may decrease spatiotemporal resolution. Therefore, in such systems reliable validation of strain data is questionable.

3) There is a significant inter-vendor variability.

Cardiac magnetic resonance imaging (MRI):

This is considered as gold standard for assessment of left ventricular systolic function. Cardiovascular magnetic resonance imaging is highly accurate, well validated and reproducible technique for assessment of ventricular volumes, function and mass. It includes not only systolic function but diastolic function also. This provides an insight into the complex changes in ventricular morphology, physiology and function in cardiovascular disease. This has produced a great interest not only in research field but also as an important clinical tool(17).

Importance of speckle tracking echocardiography derived global strains in various conditions:

Lot of studies have proven that speckle tracking echocardiography derived global strain provides more prognostic information beyond LV ejection fraction in following conditions:

1) Coronary artery disease: The subendocardium of left ventricle is the most vulnerable area that is affected by hypoperfusion and ischemia(18). So, left ventricle longitudinal mechanics may therefore be altered in patients of CAD. Choi et al(19) showed that a cutoff value of -17.9% for mid and basal peak longitudinal strain can discriminate severe triple vessel or left main CAD from patients with CAD of lesser severity with a specificity of 79.3% and sensitivity of 79.3%.

2) Myocardial infarction: STE derived global strains have increased the specificity and sensitivity for determining the size of infarct. Using a cut off value of -15% infracted segments could be detected with a specificity of 95% and sensitivity of 76% at segmental level and 93% and 83%, respectively, at global level(20). 2D STE derived circumferential and radial strains can be used to detect extent of infarction(21).

A segmental radial strain cutoff value of 16.5% could distinguish transmural infarcts from nontransmural with a specificity of 71% and sensitivity of 70%(21). Circumferential strain had a cutoff of < -11% to distinguish transmural from nontransmural with a specificity of 71.2% and sensitivity of 70.4% (21).

3) Revascularization: 2D STE derived strains can be used in predicting myocardial segments with resting dysfunction that will likely to improve after revascularization (22). Park et al (23) found that GLS of < -10.2% following reperfusion therapy in patients of acute anterior wall myocardial infarction predicted the nonviable myocardium with sensitivity of 90.9% and specificity of 81.8%. In the study, they showed that GLS of < -6.4% predicted death or development of heart failure with a specificity of 84.6% and 81.8%.

4) Valvular heart disease: In aortic stenosis patients, 2D STE derived GLS can detect subclinical dysfunction and has prognostic incremental value over other traditional risk factors for aortic stenosis like class of symptoms, mean and peak gradients, and ejection fraction(24). However, circumferential and radial strains have shown to be normal in severe aortic stenosis patients(25).

Aortic regurgitation is characterized by increase in end diastolic volume and preload. Ventricular dilatation and remodeling can masks the clinical LV dysfunction(26). 2D STE derived GLS is reduced in mild aortic regurgitation patients with normal LV systolic function(27).

2D STE derived GLS, GCS and GRS all has been reported to be less in patients of mitral regurgitation with preserved LV systolic function(28).

5) Physiological hypertrophy: Several 2D STE derived global strain studies have attempted to decipher the complex changes in LV mechanics seen with exercise. Most of the studies have found a significant increase in strains and development of a higher regional function reserve during high intensity training(29).

6) Hypertensive heart disease: It is characterized by cardiac hypertrophy in response to increased cardiac after load, followed by progressive fibrosis of myocardium. STE derived GLS is reduced in hypertension while LV circumferential and radial strains are very well preserved(12). Beta blocker therapy can lead to adaptation in LV systolic mechanics such that a reduction in longitudinal strain is associated with improvements in circumferential strain and stroke volume(30).

7) Hypertrophic cardiomyopathy: Hypertrophic cardiomyopathy is characterized by myocardial fibre disarray, which results in LV systolic and diastolic dysfunction. Two dimensional speckle tracking derived global longitudinal strain is reduced in patients with hypertrophic cardiomyopathy in proportion to symptoms of patient(31).

   The location and amount of left ventricular fibrosis and end diastolic posterior wall thickness are independent predictors of global longitudinal strain(32).

   Depending on extent of hypertrophy, the extent of compensation done by circumferential strain may vary in relation to longitudinal strain(33).
   In apical hypertrophic cardiomyopathy, Reddy et al(34) found that there is progressive increase in longitudinal strain from base to apex.

8) Dilated cardiomyopathy: In idiopathic dilated cardiomyopathy, generally all global strains are reduced in accordance with left ventricle ejection fraction(35).

9) Stress cardiomyopathy: The most common type of stress cardiomyopathy is apical ballooning syndrome. Two dimensional speckle tracking derived global strains have shown that reduction of left ventricular strains in a segmental territory that extends beyond any single vascular distribution pattern(36).

   Baccouche et al(37) have shown that apical ballooning syndrome patients have hyperkinesis in basal region, hypokinesia in mid left ventricular level and dyskinesis at apex in terms global longitudinal strain. So, in genral strain abnormalities in apical ballooning syndrome does not follow a single vascular territory which can be helpful in differentiating from acute coronary syndrome.

10) Pericardial disease: In constrictive pericarditis, two dimensional derived global circumferential strain and twist are significantly reduced while global longitudinal strain is preserved(38).

11) Chemotherapy induced LV systolic dysfunction: In patients who receive cardiotoxic chemotherapy, changes in 2D STE derived GLS can precede decrease in ejection fraction and segmental changes in mid and apical GLS suggest an increased chances of decreased EF in future. GLS

can also be used for serial clinical monitoring of cardiotoxic chemotherapy(39).

12) After cardiac surgery : GLS has proven its incremental value over LV ejection fraction for risk stratification in patients who underwent cardiac surgery for different indications like coronary artery bypass grafting, aortic valve replacement , and mitral valve surgery(40).

13) Post cardiac transplant: Early assessment of 2D derived STE may be a good predictor of one year mortality in post cardiac transplant patients(41).

14) Heart failure syndromes: Conventional concepts of heart failure have largely been limited to hemodynamic consequences of LV systolic dysfunction. Using a time dependent model of heart failure, it has been proposed that diastolic and systolic heart failure are phenotypic expressions of same disease process that evolves gradually as a continuum of clinical events(42).

Assessment of cardiac mechanics by speckle tracking echocardiography has uncovered this continuum of heart failure. Patients with diastolic heart failure have decreased two dimensional STE derived global longitudinal strain which co-relates with increased risk of heart failure events(43). However, radial and circumferential strain patterns may vary in diastolic heart failure patients(44).

15) Assessment before cardiac resynchronization therapy: Speckle tracking derived global strains have fuelled interest in assessing left ventricular mechanical function. Speckle tracking echocardiography has allowed assessment of circumferential and radial components of myocardial motion for dyssynchrony analysis in determining response to cardiac resynchronization therapy, including extent of left ventricular dyssynchrony and presence of contractile reserve(45). Despite advances, there is no consensus on how LV mechanics should be assessed before going for cardiac resynchronization therapy.

16) Diabetes: Subclinical longitudinal dysfunction is frequently observed in asymptomatic diabetes patients with normal left ventricular ejection fraction. The decrease in longitudinal strain co-relates with duration of diabetes(46). So, two dimensional derived strain has potential for detecting subclinical LV

systolic dysfunction and might provide useful information of the risk stratification in asymptomatic diabetic population.

17) Amyloidosis: 2D STE derived strain has a crucial role in early diagnosis and prognostic evaluation in cardiac amyloidosis patients(47). Longitudinal myocardial strain as derived by TDI has demonstrated that it was reduced at the base and mid myocardium sparing the apex in asymptomatic cardiac amyloidosis patients with or without hypertrophy(48). However, TDI has limitations of angle dependence and noise interference. Speckle tracking echocardiography overcomes these limitations. Sun et al(49) have reported that global longitudinal, radial, and circumferential strain detected by 2D STE were significantly lower in cardiac amyloidosis, hypertrophic cardiomyopathy, and hypertensive heart disease. Recently Quarta et al(50) have demonstrated that myocardial deformation derived by 2D STE global longitudinal strain in patients of cardiac amyloidosis was severely impaired at mid and basal LV segments while apical longitudinal strain (Figure-1) was preserved irrespective of degree of wall thickening and etiology of cardiac amyloidosis. It produces a cherry dot sign on final bull's eye report suggesting apical sparing (figure-2).

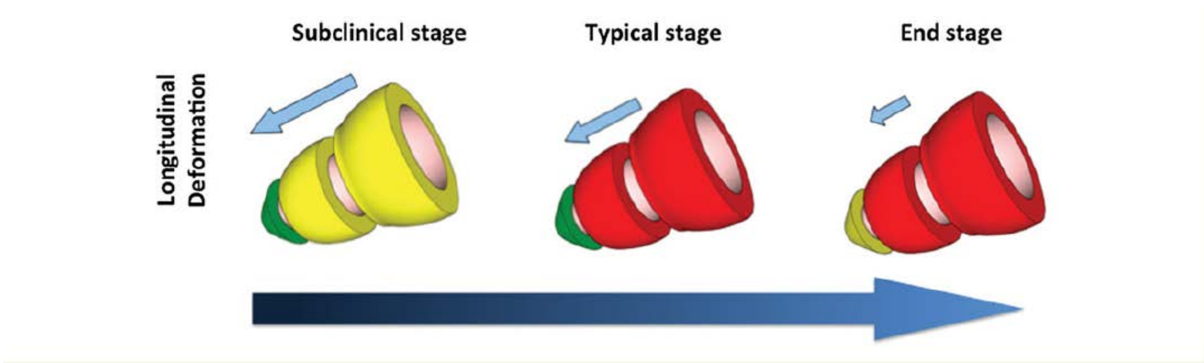

Figure-1: Myocardial deformation in different stages of cardiac amyloidosis.

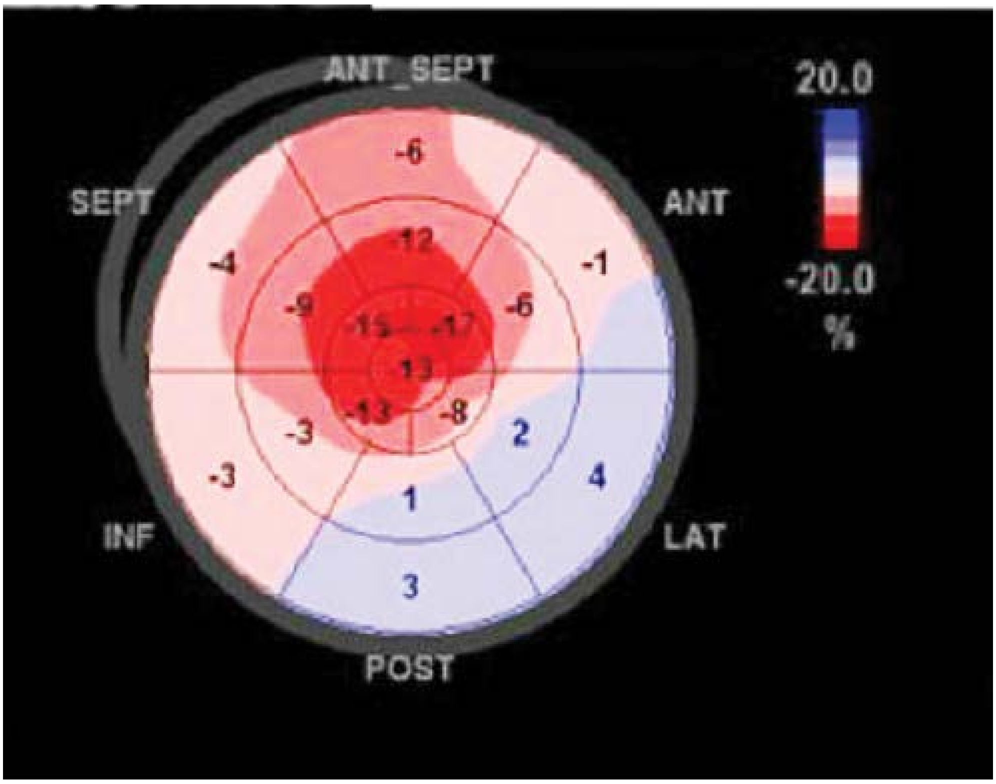

Figure-2: Severe impairment of global longitudinal deformation with lower deformation in basal segments in comparison to apical segments (Cherry dot sign)

MATERIALS AND METHODS

This observational study was done in 100 patients with LV systolic dysfunction (defined as patient with EF less than 50%) from cardiology inpatient and outpatient.

Exclusion criteria:

1) Poor Echo window

2) Patients with atrial fibrillation/atrial flutter/frequent ectopics

3) Patient below 18 years

4) Consent not given

5) Unstable clinical condition

Inclusion criteria:

Patients with LV systolic dysfunction (defined as patient with EF less than 50%) were taken into the study after written consent.

All the patients underwent detailed Echocardiography with 2D speckle tracking and 3D echocardiography. Baseline characteristics of patients were noted. Variables were 2 D EF, 3D EF, 2 D global longitudinal strain and 2 D global circumferential strain

Data Sources/measurement:

ECHO: Patients were recruited into study from echo room from cardiology department. Each individual enrolled in this study underwent transthoracic Echo in left lateral decubitus position in expiratory apnoea by 5-1 Hz Matrix probe on IE 33(Philips Medical System).

Standard 2D echocardiographic images were obtained in parasternal long axis and short axis views, apical 4 chamber view, apical long axis view and apical two chamber view with ECG. For 3D echocardiography, images were acquired in full volume mode in expiratory apnoea to remove the lung field coming over anterior wall of left ventricle.

2D ejection fraction was calculated using biplane Simpson's method (Figure-3). LVEF was calculated and expressed as percentage.

Using 2D speckle tracking echocardiography, global longitudinal strain was calculated in offline mode in apical four chamber view (figure-4), apical long axis (Figure-5) and apical two chamber view (Figure-6). For 2D STE global circumferential strain, three views in parasternal short axis at basal level (Figure-7), parasternal short axis at papillary muscle level (figure-8) and parasternal short axis apical view were acquired (Figure-9). Endocardial borders were tracked by automatically using software named as QLAB and a region of interest was selected that includes the entire myocardium. If these were not accurate, then manual tracking of endocardial border was done. Results of the LV strain analysis were automatically displayed as a seventeen segment polar map model (Figure-10) with seventeen regional strain values and a meal global value for the entire myocardium.

For 3D ejection fraction calculation (Figure-11), 3DQ Adv software was used. Endocardial borders were tracked manually after adjusting images in three axes (apical four chamber, apical two chamber and short axis). End diastolic and end systolic images were decided according to Electrocardiogram (ECG). End diastolic was taken at peak of R wave and end systolic was taken at the end of T wave. All the parameters were recorded in accordance with the guidelines from the American Society of Echocardiography. Patient's baseline characteristics in the form of age, sex, body surface area, diabetes, hypertension, dyslipidemia, smoker, coronary angiogram and etiology of LV dysfunction were noted.

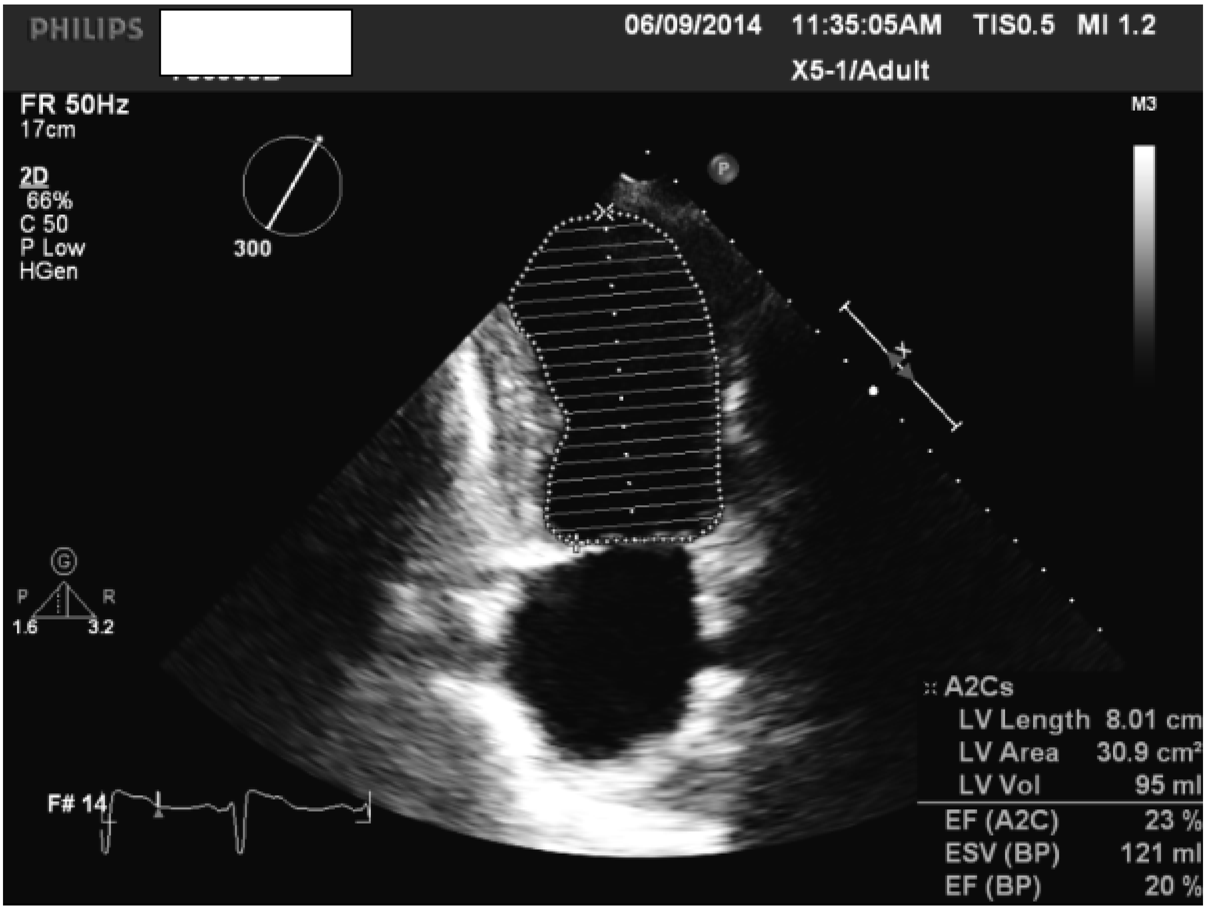

Figure-3: 2D ejection fraction calculation using Biplane Simpson's method.

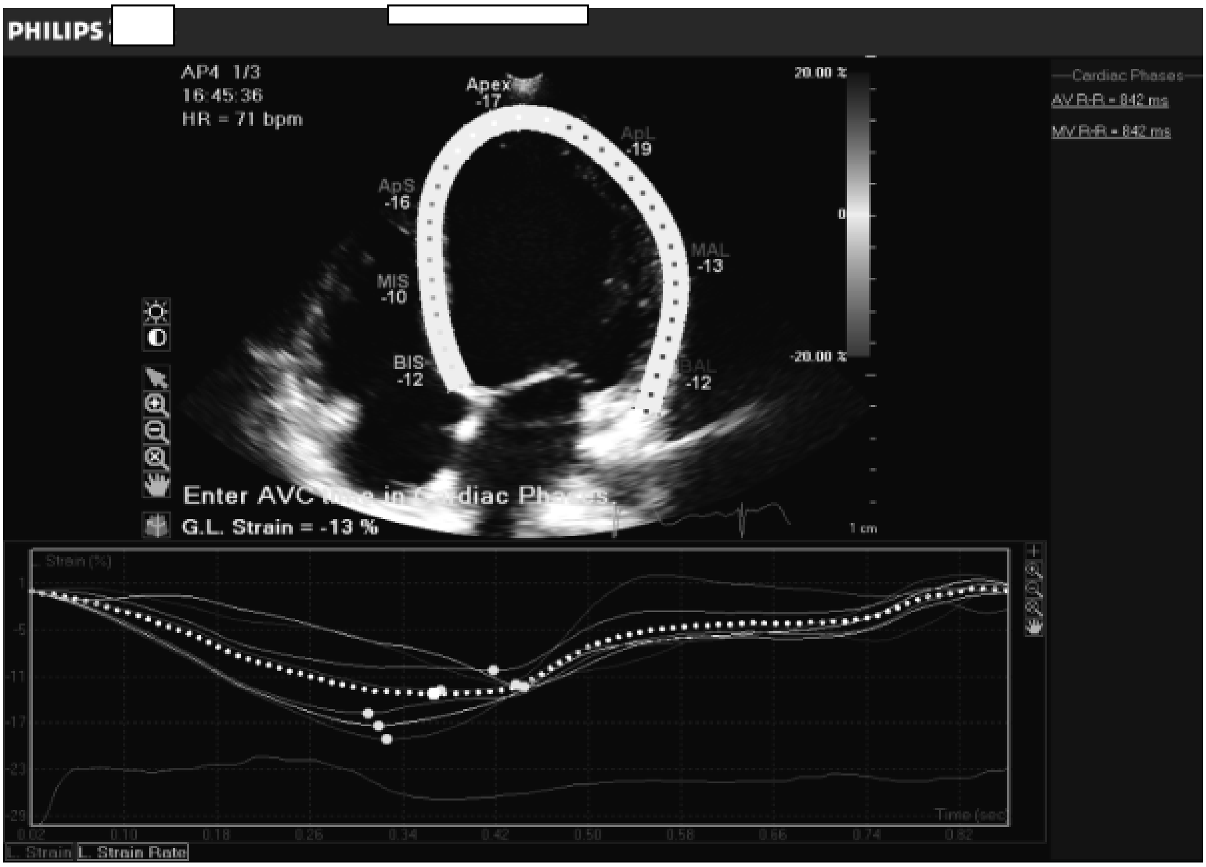

Figure-4: Global longitudinal strain apical 4 chamber view

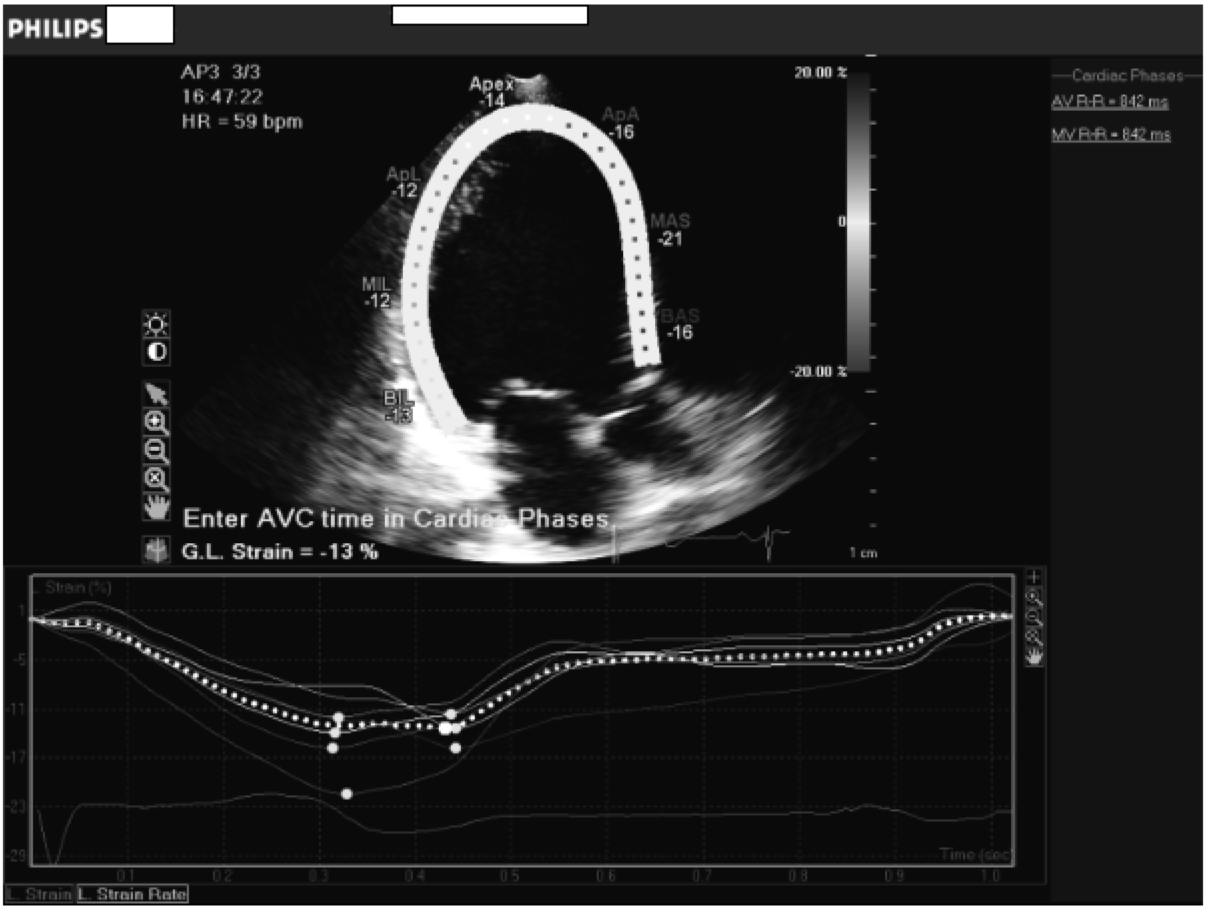

Figure-5: Apical long axis view for global longitudinal strain

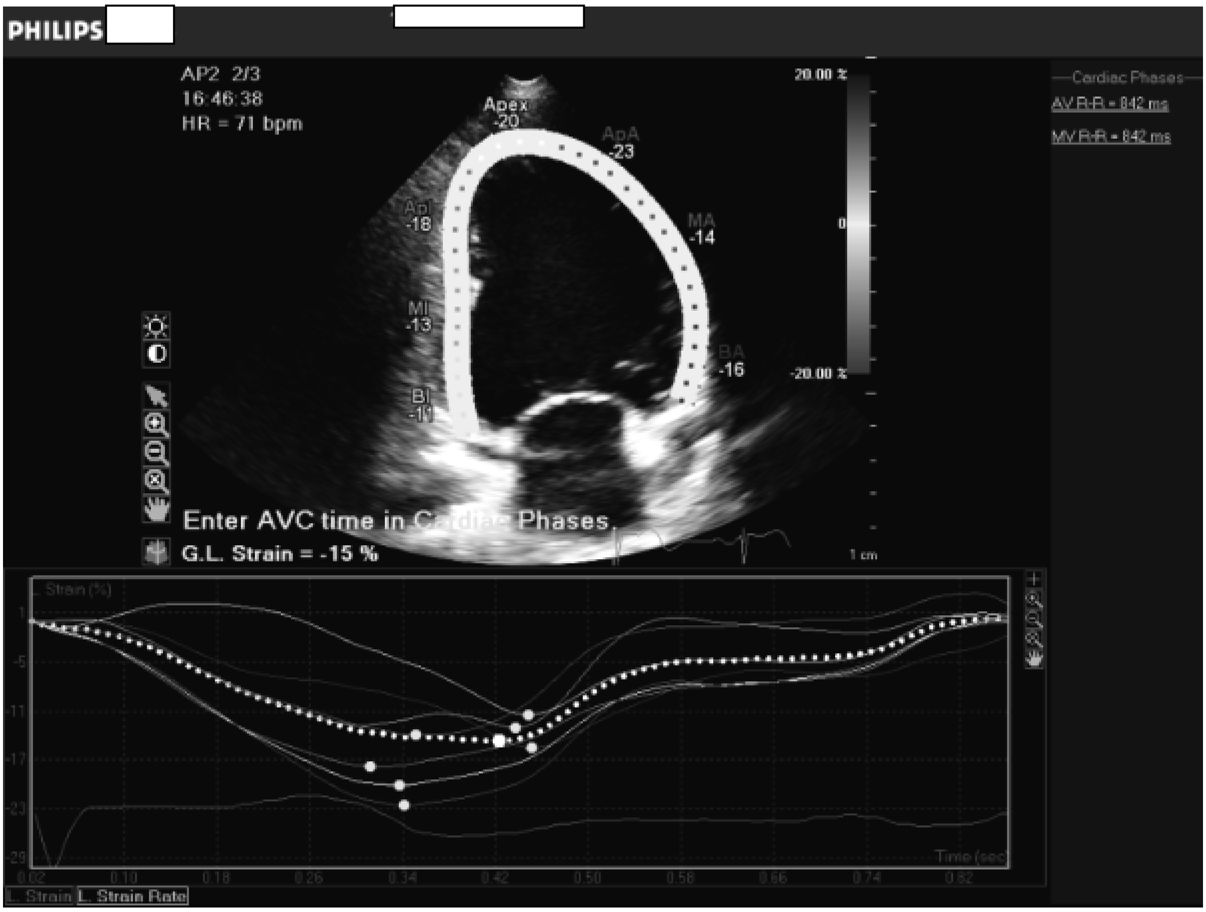

Figure-6: Apical two chamber view for global longitudinal strain

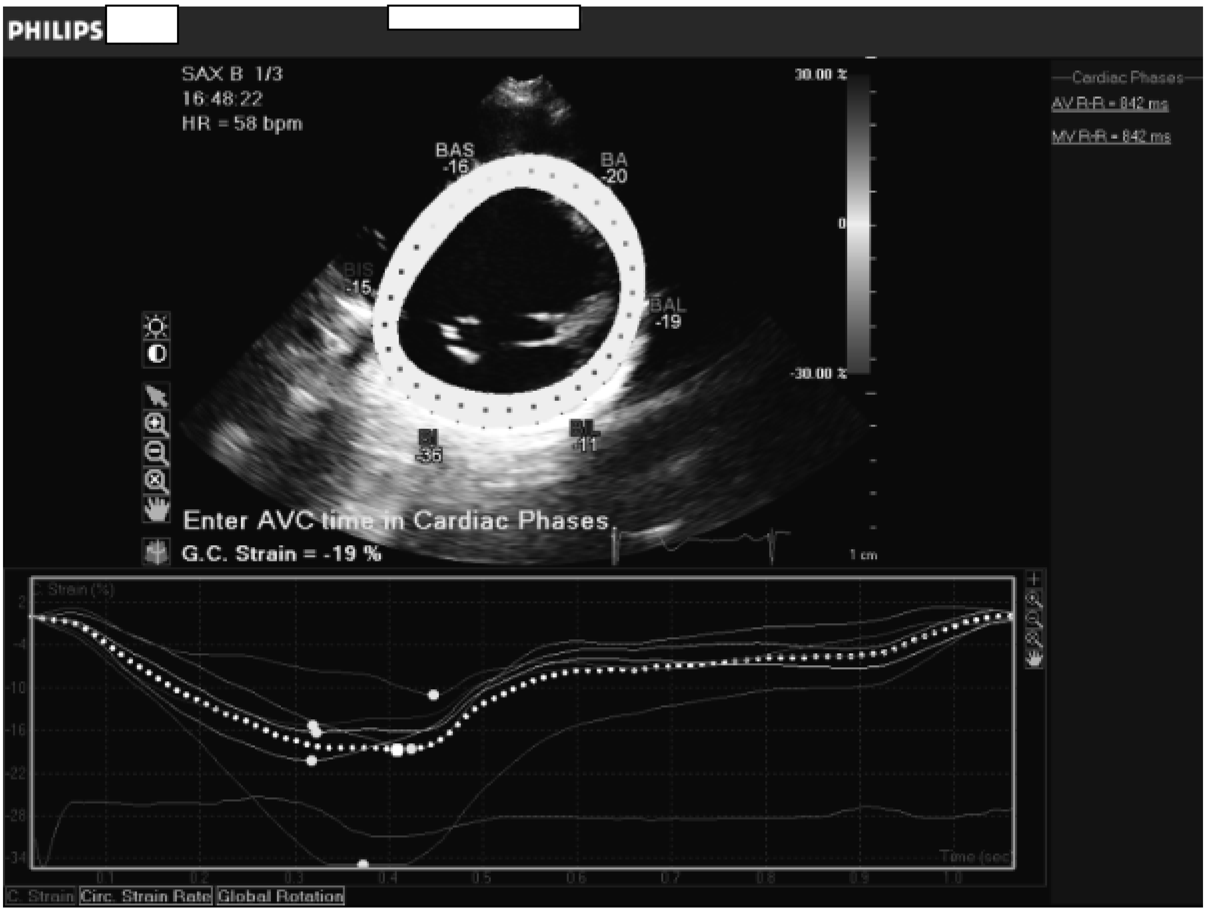

Figure-7: Parasternal short axis view for global circumferential strain

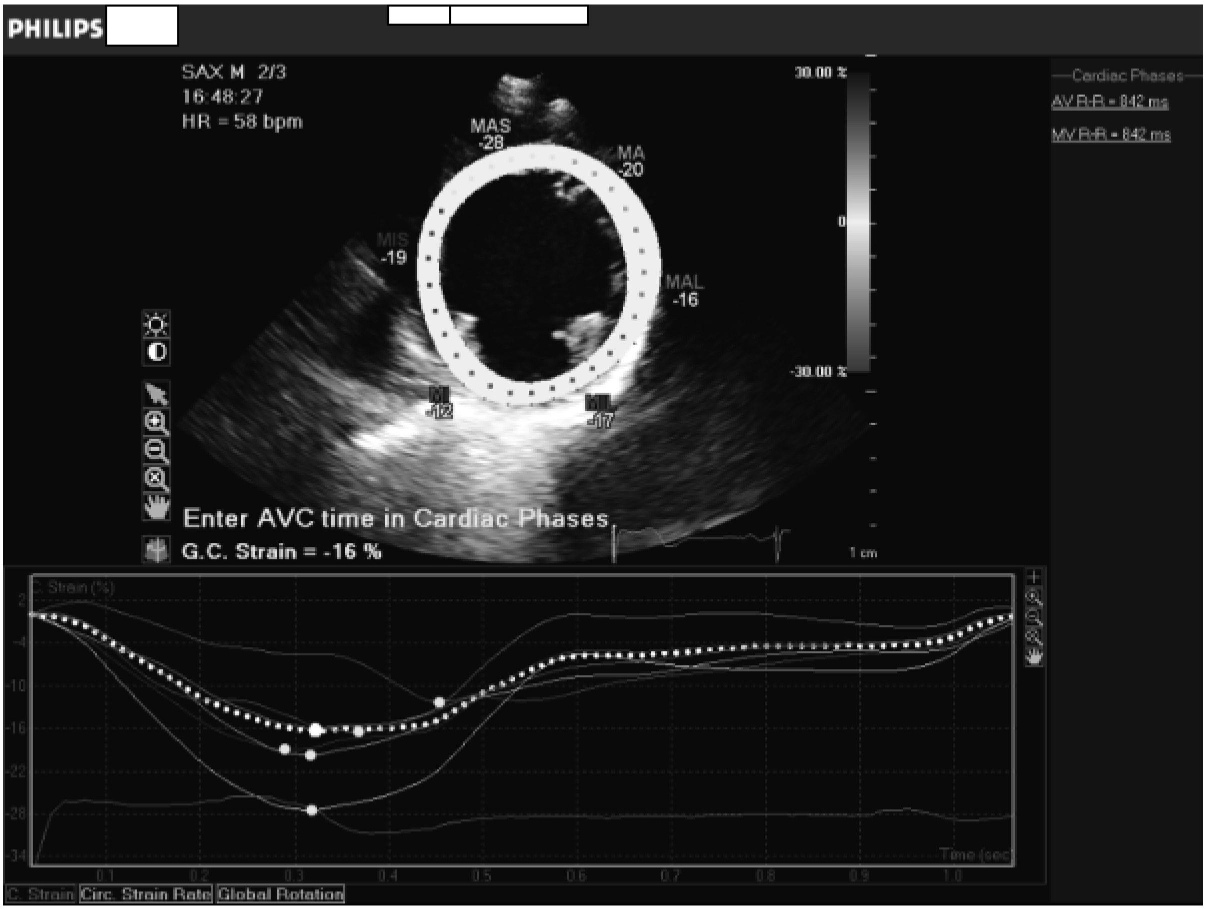

Figure-8: Parasternal short axis view at papillary muscle level for global circumferential strain

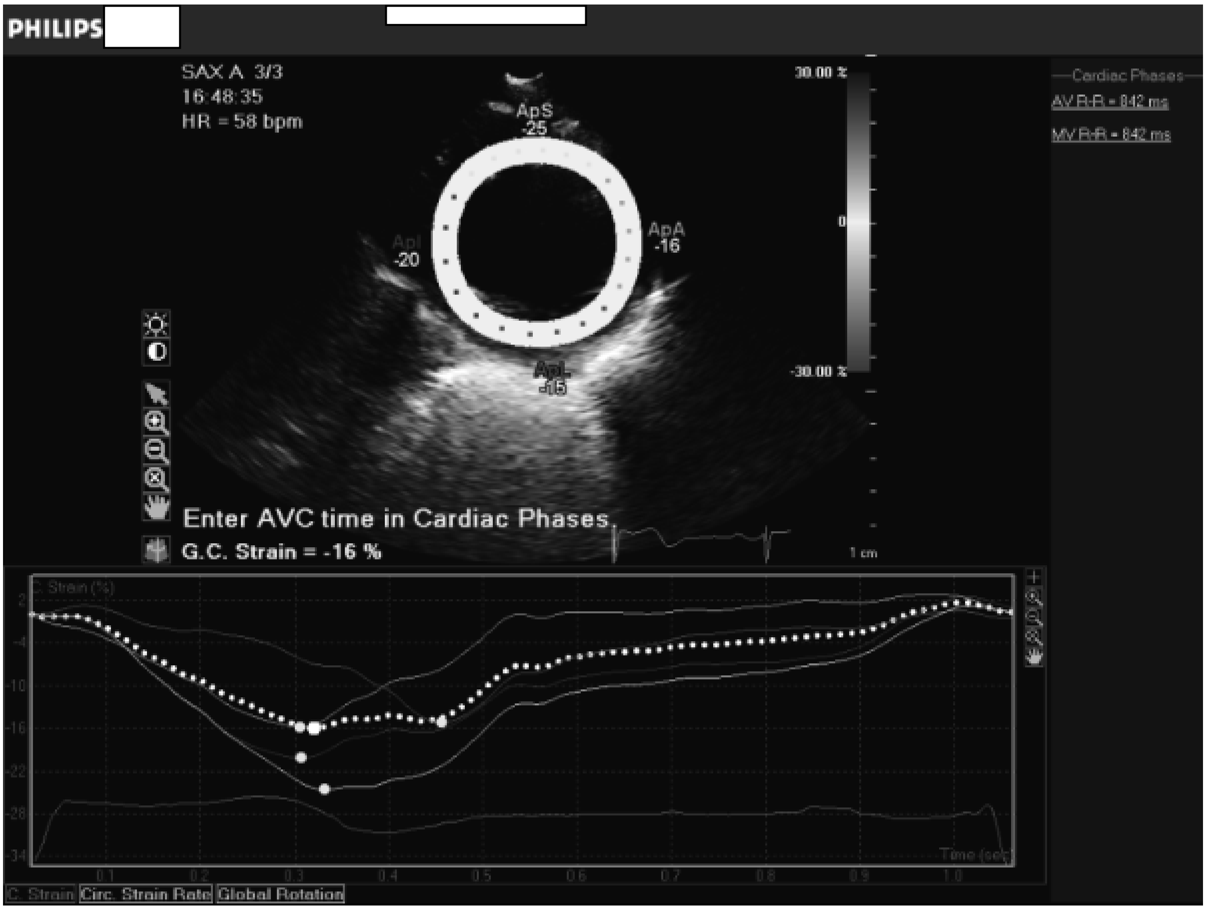

Figure-9: Parasternal short axis view at apical level for global circumferential strain

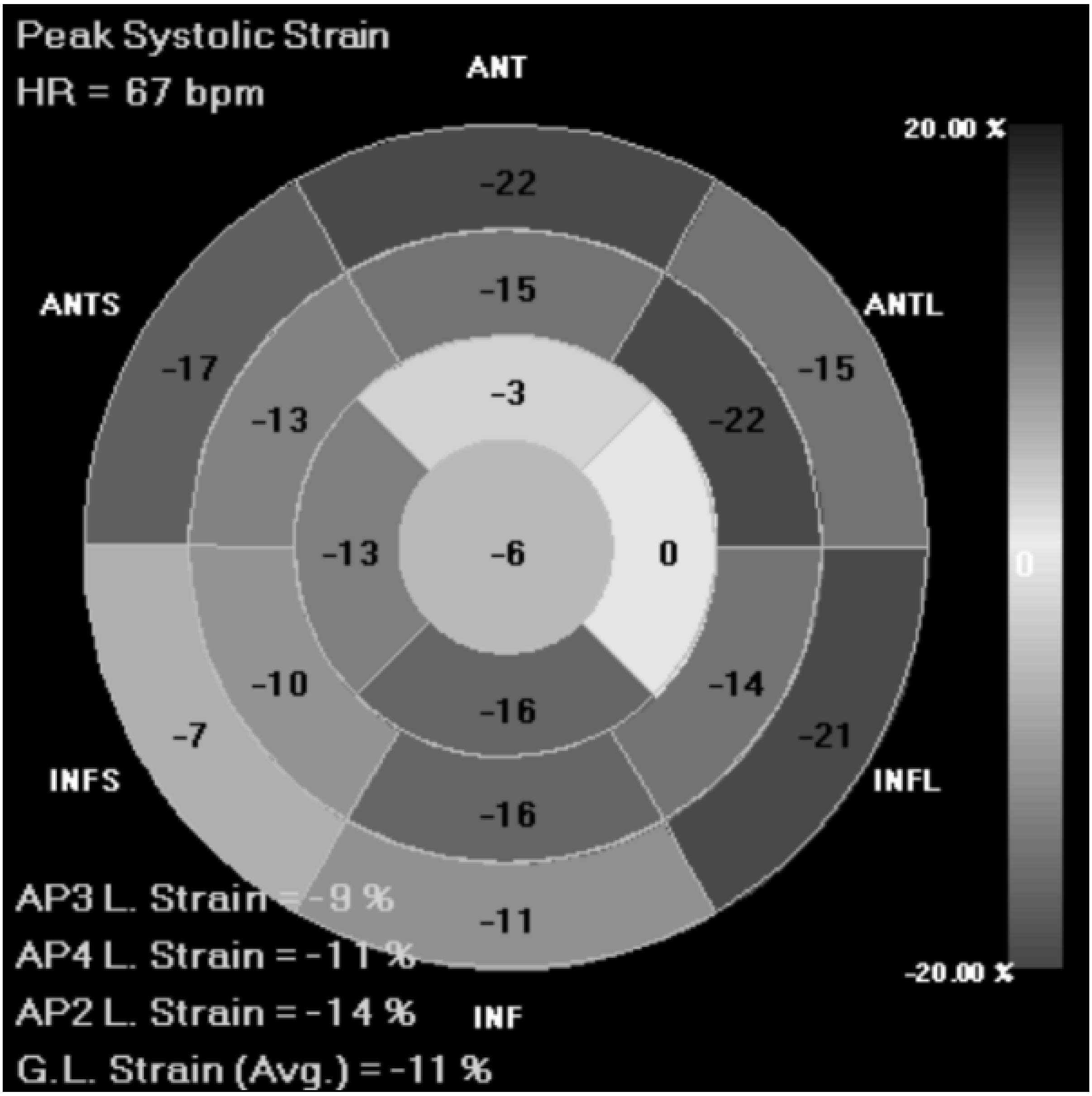

Figure-10: Bull's eye map for GLS

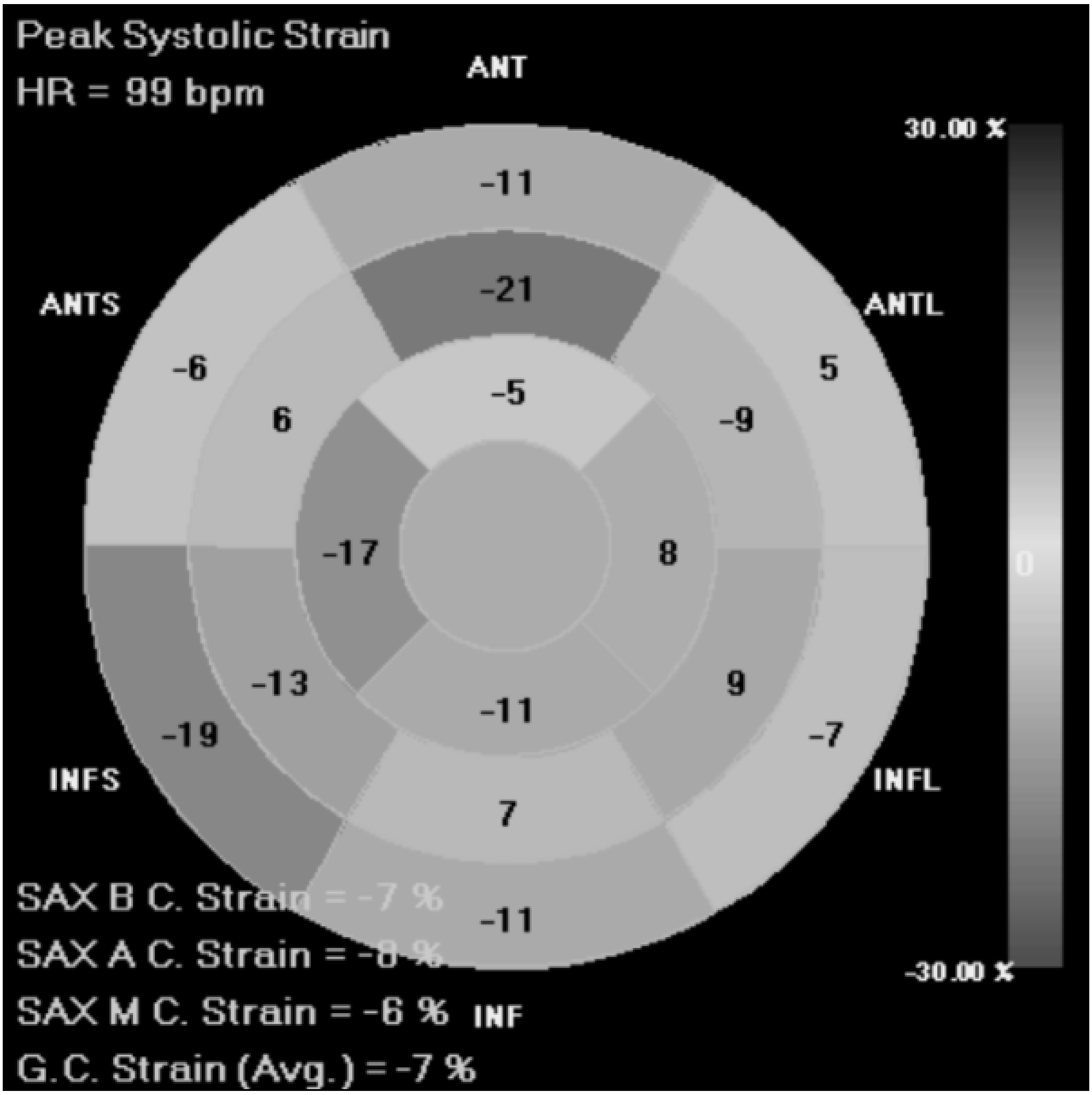

Figure-11-Bull' eye map for GCS.

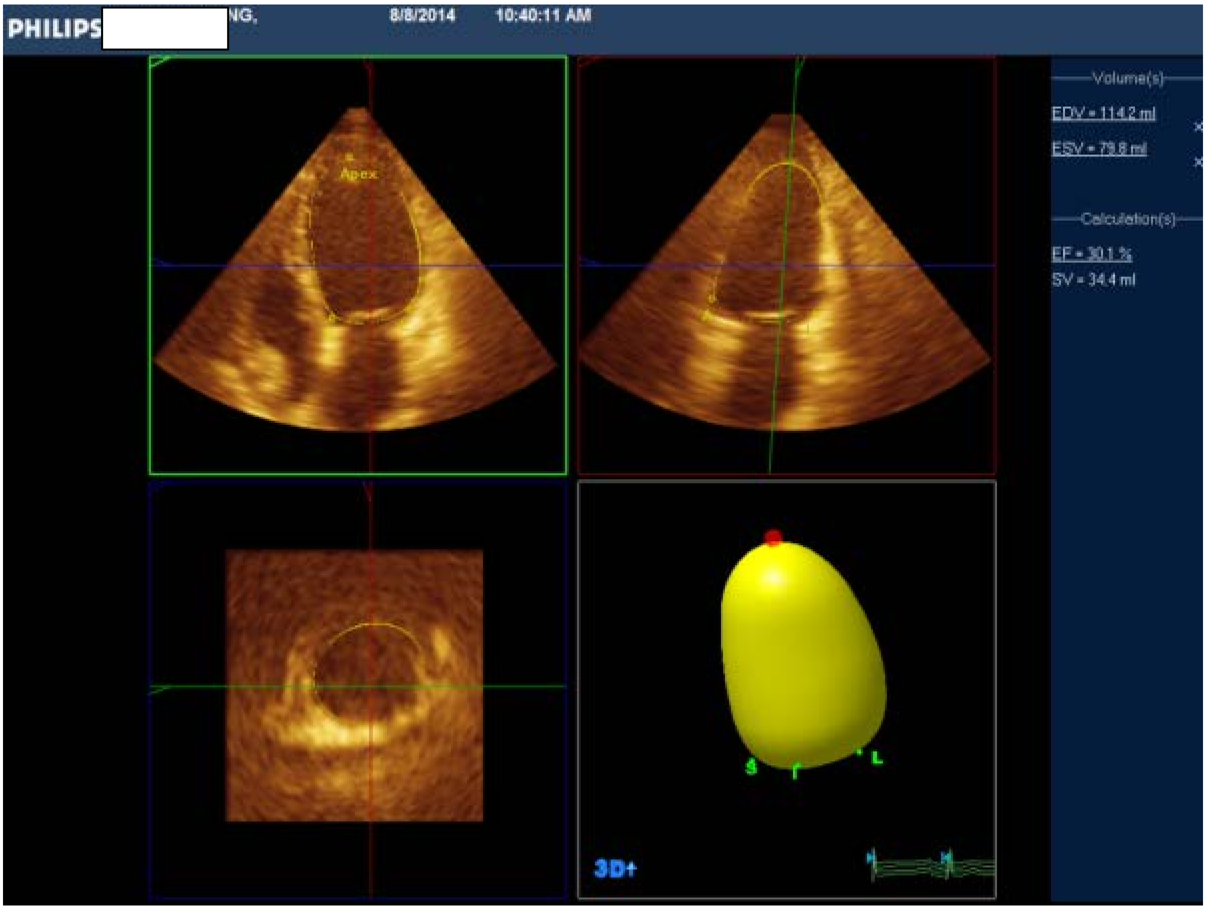

Figure-12: Calculation of three dimensional ejection fraction using 3d Adv software.

Data collection and analysis:

The data was entered in EPIDATA software and analyzed using SPSS 19.0 (Chicago, IL, USA). Continuous variables were expressed as mean +/- SD or as percentages. Correlation between strain measurements and LVEF was assessed using linear regression analysis with Pearson's correlation coefficient. P values < 0.05 using a two sided test was considered as significant.

Intra-observer and inter-observer variation in measuring 2 D global strain and 2 D ejection fraction and 3 D ejection fraction were measured using Coefficient of variation, intra-class correlation coefficient and standard error of measurement .Ten cases were randomly selected for inter-observer and intra-observer variation. Inter-observer variation was calculated between myself and my guide without knowing the earlier results. Intra-observer variation is calculated offline one week apart with blinding to earlier result.

Sample size:

Based on earlier studies, which have shown a correlation coefficient of 0.86 for comparing 2D GLS with 2 D EF and 3D EF, Sample size calculation is as follows:

Regression methods - Sample size for correlation coefficient analysis (testing against population value)			
Sample correlation coefficient	0.86	0.86	
Population correlation coefficient	0.6	0.05	
Power (1- beta) %	90	90	
Alpha error (%)	5	5	
1 or 2 Sided	2	2	
Required sample size	32	10	

Detailed diagrammatic algorithm of study

Observational study
In
Department of Cardiology

LV systolic dysfunction

Exclusion criteria:

1) Poor Echo window

2) Patients with atrial fibrillation/atrial flutter/frequent ectopics

3) Patient below 18 years

4) Consent not given

5) Unstable clinical condition

Inclusion criteria:

1) Patient having LV systolic dysfunction (defined as patient with EF less than 50%) of varied etiology.

Primary outcomes of study

RESULTS

BASELINE CHARACTERISTICS:

A total of 100 patients with LV systolic dysfunction were taken into the study. Mean age of patients in study population was 50 ± 12.4 years. Ratio of Male: Female in my study was 3: 1, 44% of total study population were diabetics, 37% had hypertension, 18% had dyslipidemia, 31% were current smoker. Out of 100 patients only 50 patients has undergone coronary angiogram, out of which 13 patients had normal coronaries, 13 patients had single vessel coronary artery disease(CAD),14 patients had double vessel CAD, 10 patients had triple vessel CAD or left main CAD. 56% patient had LV dysfunction due to ischemic etiology and 44% had other etiology of LV dysfunction like chronic kidney disease, post chemotherapy and dilated cardiomyopathy.

Table-1: Baseline characteristics.

Variables	Value
Age(years)	50 ± 12.4
M:F	3:1
BSA(m2)	1.63±0.23
Heart rate (beats/min.)	70±12
Diabetes	44%
Smoker	31%
Hypertension	37%
Dyslipidemia	18%
Ischemic heart disease	56%
Others etiology	44%

Most of the patients taken in this study were in the age group of 40-60 years.

This study has maximum middle age population

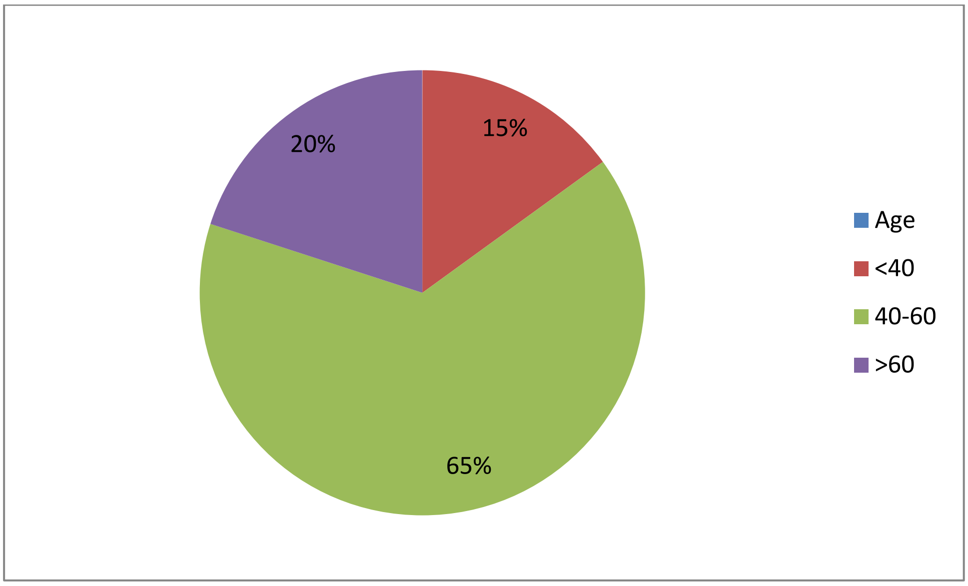

Figure- 12: Age distribution in the study. Age in years

Most of the patients taken into the study were males in the ration of 3:1.

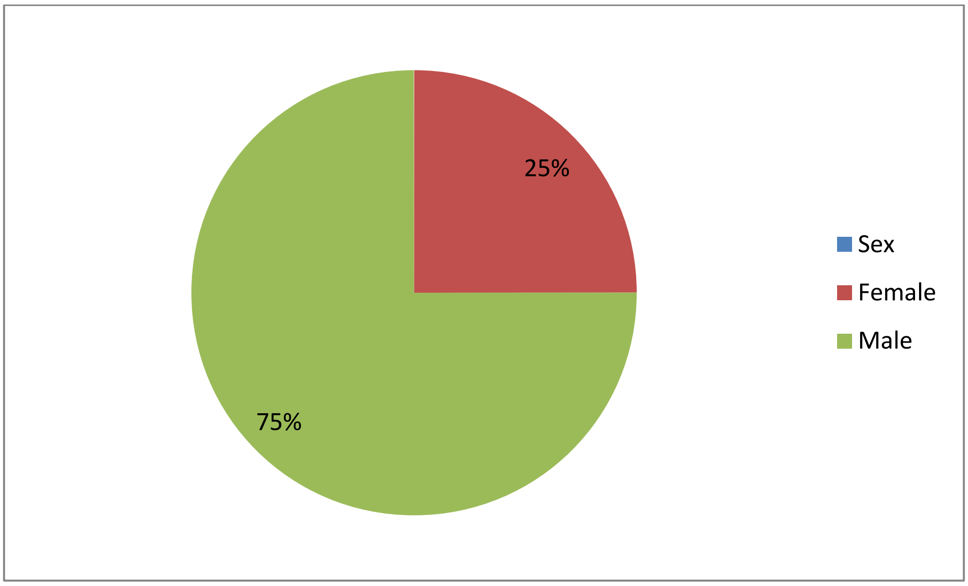

Figure- 13: Sex distribution in the study.

Only 50 out of 100 patients had a coronary angiogram done before coming to Echo room. Minor coronary artery disease defined as stenosis less than 50% and significant coronary artery disease as stenosis more than 50%. Out of 13 had normal coronaries or minor coronary artery disease, 13 patients had single vessel CAD, 14 patients had double vessel CAD and 10 patients had triple vessel CAD or left main disease.

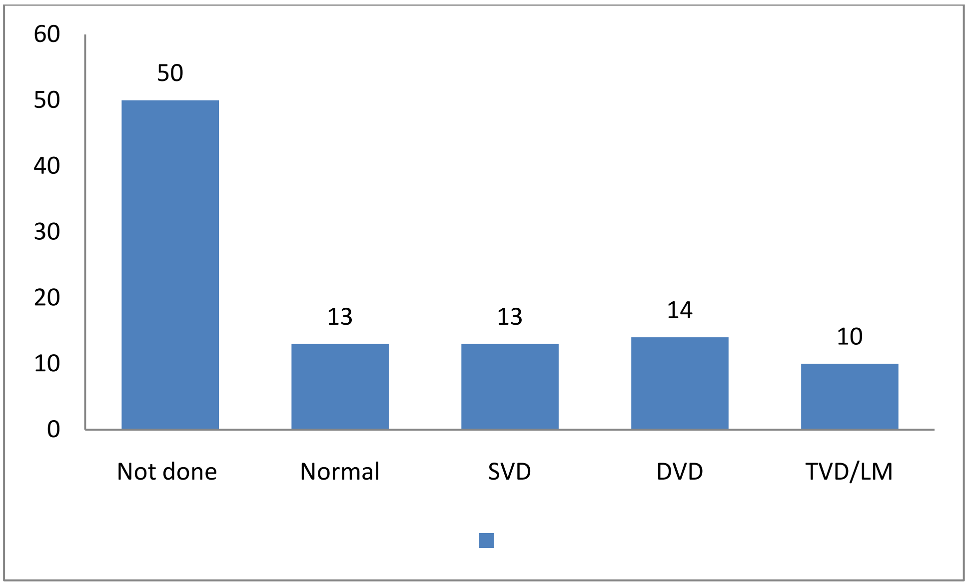

Figure- 14: Types of CAD in the study.

SVD=Single Vessel CAD,DVD=Double vessel CAD,TVD/LM= Triple vessel CAD/Left main

Most of patients taken in to study were smokers (69%). Smokers were defined as who was either current smoker or had left smoking in last two years.

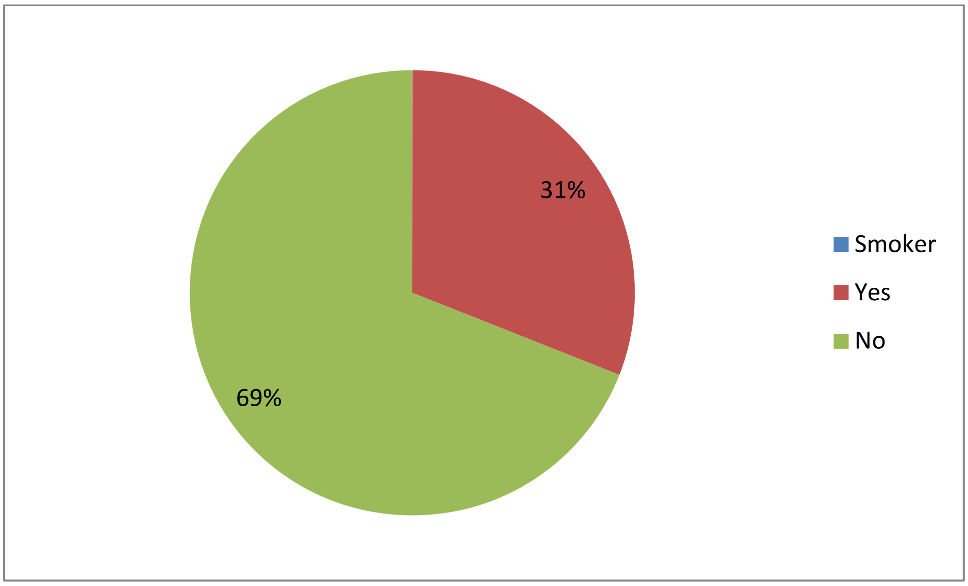

Figure- 15: Smoker vs non smoker in the study.

Most of the patients taken into study were non-hypertensive. Hypertension was defined as patient who has blood pressure ≥ 140/90 or on antihypertensive medications.

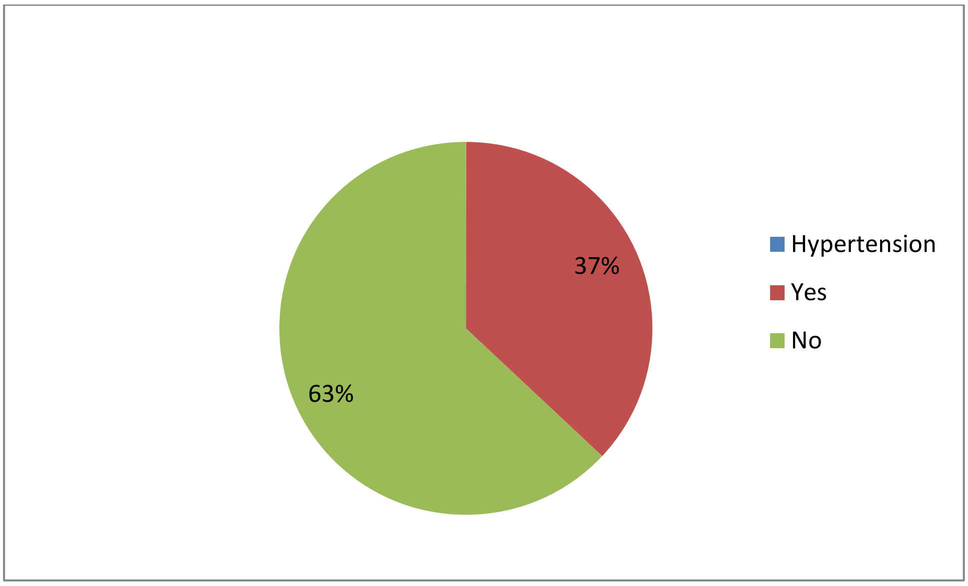

Figure- 16: Hypertension distribution in the study.

44% of the total study population was diabetic. Diabetes was defined as either patient is on oral hypoglycemics/ insulin or patient is having fasting blood sugar more than 126mg/dl or blood sugar 2 hrs after food is ≥ 200mg/dl or HbA1c ≥ 6.5gm/dl or random blood sugar of 200mg/dl with symptoms of polyuria/polydypsia.

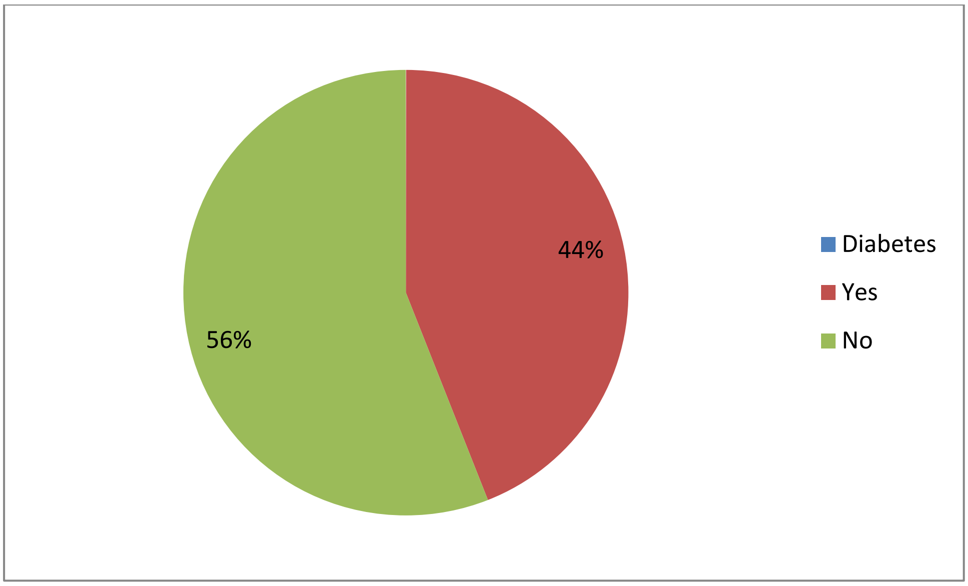

Figure 17 : Distribution of diabetes in the study.

18% of the total study population were dyslipidemic. In this study, dyslipidemia was taken as either patient is on treatment for dyslipidemia or patient whos has low density lipoprotein (LDL) ≥ 100mg% with documented CAD/diabetes mellitus/Ischemic heart disease or LDL ≥ 130mg/dl with two risk factors for CAD or LDL ≥ 160 mg/dl with one risk factor for CAD or LDL ≥ 190mg/dl.

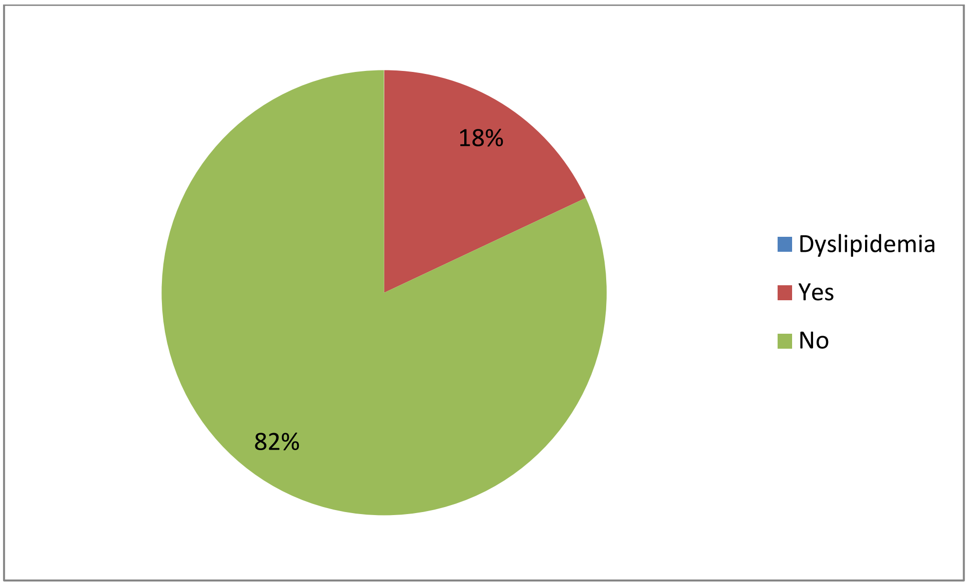

Figure-18: Distribution of dyslipidemia in the study.

Out of 100 patients with LV systolic dysfunction, 44% were due to Ischemic origin and rest had other aetiologies like dilated cardiomyopathy, chronic kidney disease, or chemotherapy induced LV systolic dysfunction. LV systolic dysfunction of ischemic origin was defined as either patient had a history of old or recent myocardial infarction or had documented significant CAD.

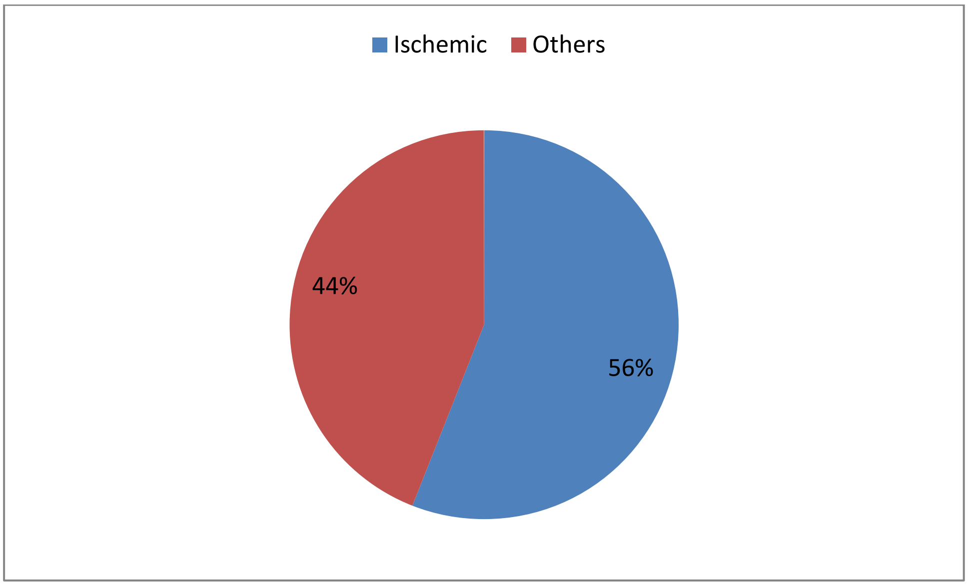

Figure-19: Distribution of etiology of LV dysfunction

Maximum End diastolic volume (EDV) was 272.9ml and minimum was 55.7ml with an average of 123.8 and standard deviation of 45.9. Maximum End systolic volume (ESV) was 200ml and minimum ESV was 31.8 with an average of 84.5 and standard deviation of 31.4. Maximum 2D EF was 49% and minimum was 20% with an average of 34% and standard deviation of 7.5%. Maximum 3D EF was 49% and minimum was 20% with an average of 34.2% and standard deviation of 7.6%. Maximum GLS value in this study was -1% and minimum was -17% with an average of -8% and standard deviation of 3.2. Maximum GCS value was -2% and minimum was -25% with an average of -10.6% and standard deviation of 4.3%.

Table-2: Echocardiographic parameters

Variable	Maximum	Minimum	Average	Standard deviation
EDV	272.9	55.7	123.8	45.9
ESV	200	31.8	84.5	31.4
2DEF	49	20	34	7.5
3D EF	49	20	34.2	7.6
GLS	-1	-17	-8	3.2
GCS	-2	-25	-10.6	4.3

Most of patients in this study had end diastolic volume(EDV) in between 100-200ml (68%). So, we did not include severely dilated left ventricle into the study.

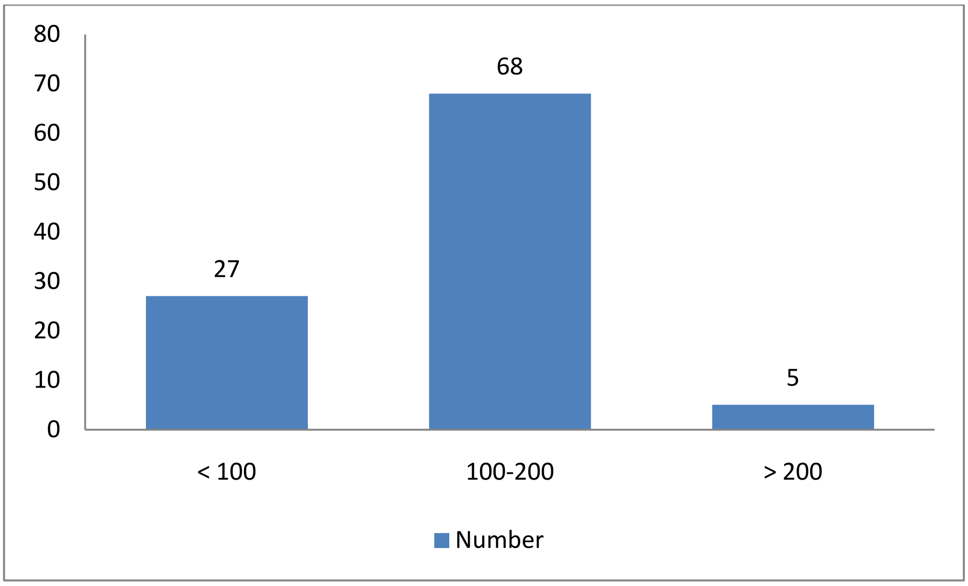

Figure-20: Distribution of patients according to EDV. EDV in ml.

Same distribution followed for end systolic volume (ESV) also. 79% of the total study population has end systolic volume less than 100ml

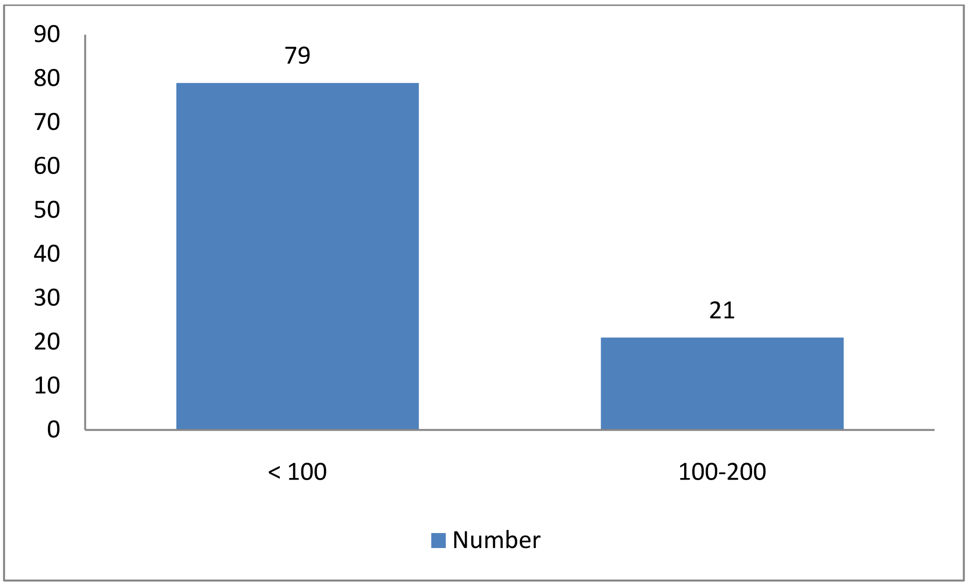

Figure-21: Distribution of patients according to ESV. ESV in ml.

31% of total study population has 2D ejection fraction less than 30%, 43% has 2D EF in between 30-39% and 26% has 2D EF in between 40-50%. As already seen in earlier studies, global strains has better co-relation at lower EF and most of study patients were in this group.

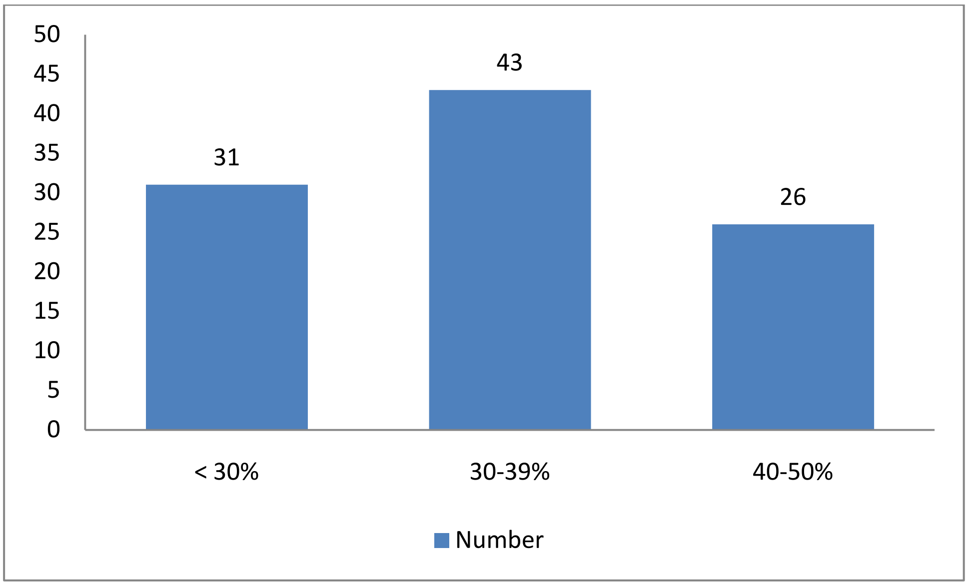

Figure-22: Distribution of patients according to various subgroups of 2D EF.

Same distribution pattern followed for 3D ejection fraction also. 46% patients had 3D EF in between 30-39.9%, 30% had less than 30% EF and 24% patient had 3D EF in between 40-50%.

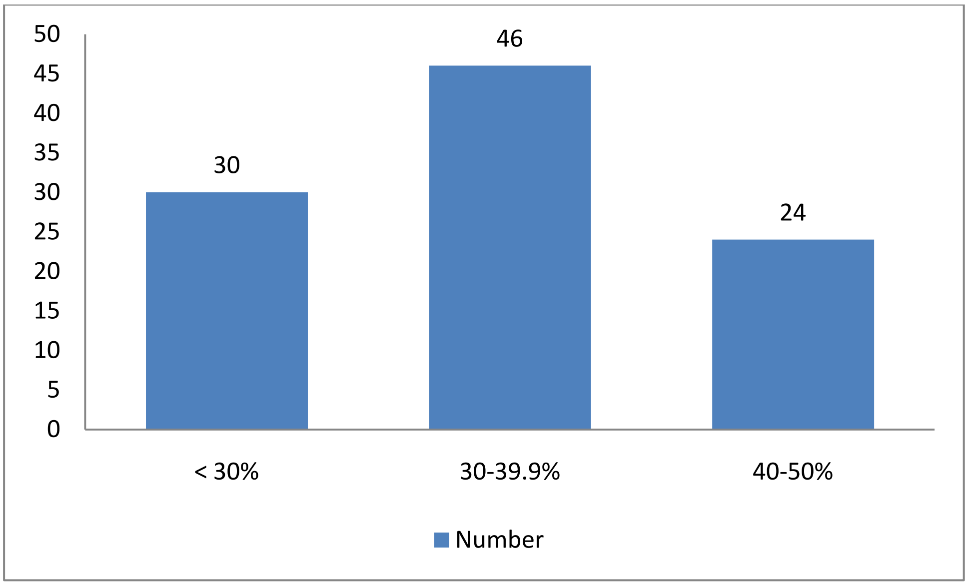

Figure-23: Distribution of patients according to various subgroups of 3D EF.

Co-relation between 2D EF and 3D EF:

Correlation between 2D EF and 3D EF was strong and Pearson correlation coefficient r, was 0.963. It was significant at the level 0.01(2 tailed).

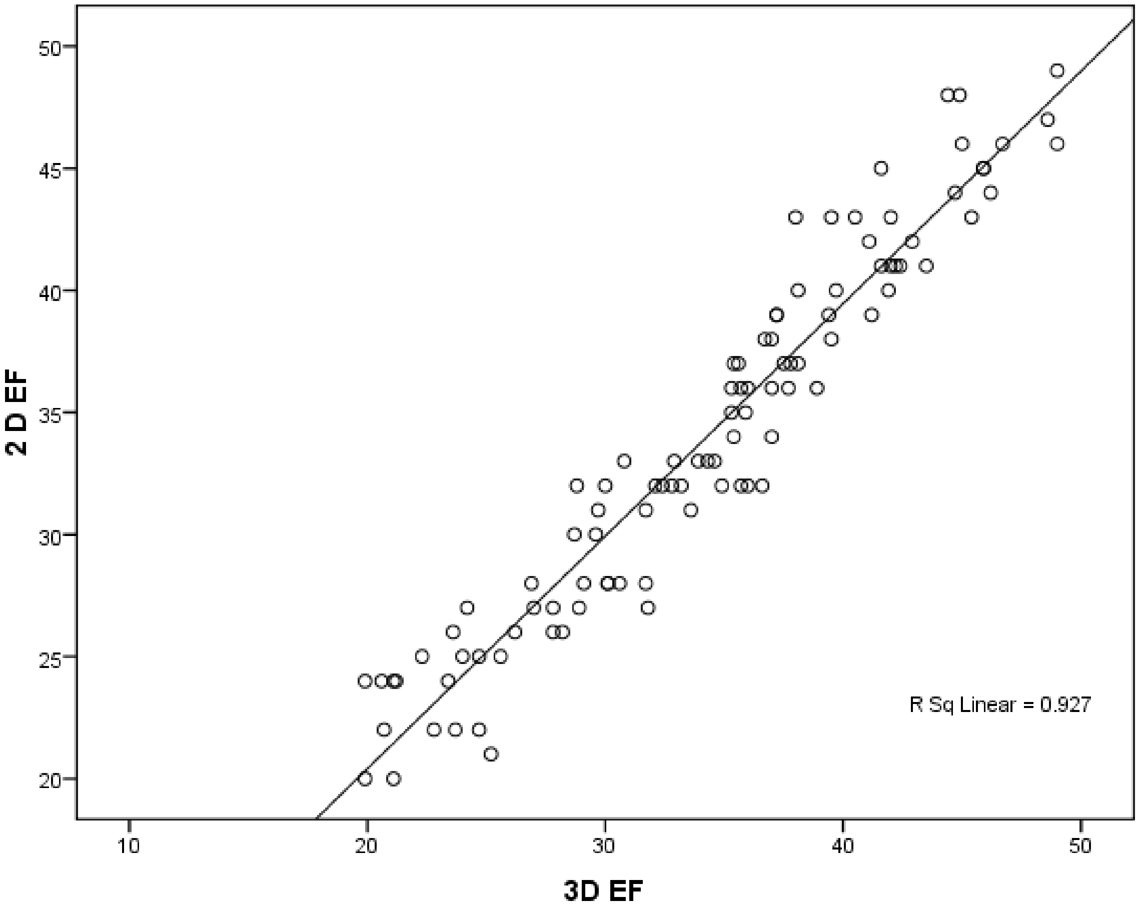

Figure-24: Scatter diagram showing co-relation between 2D EF and 3D EF.

Co-relation between GLS and 2D EF:

Correlation between 2D EF and GLS was strong and Pearson correlation coefficient r, was 0.724. It was significant at the level 0.01(2 tailed).

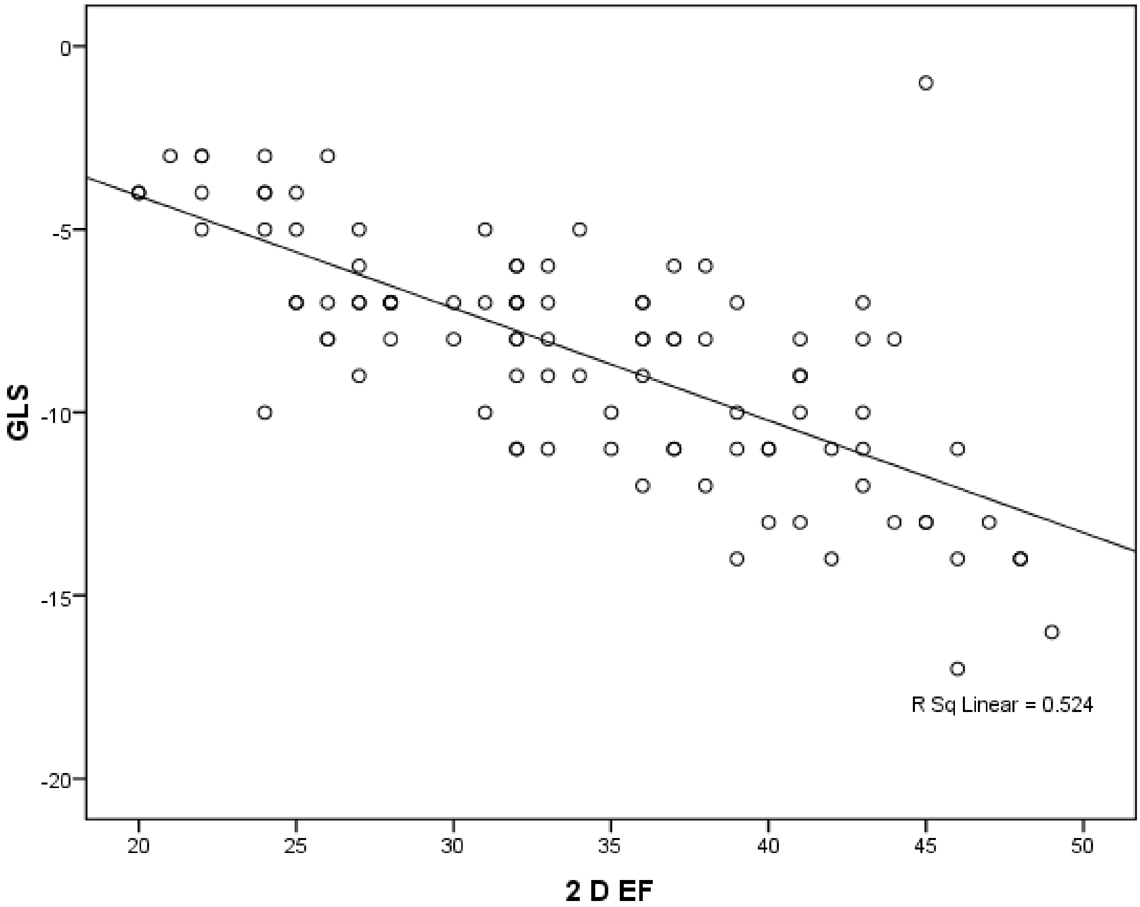

Figure-25: Scatter diagram showing co-relation between 2D EF and GLS.

Co-relation between GCS and 2D EF:

Correlation between 2D EF and GCS was strong and Pearson correlation coefficient r, was 0.652. It was significant at the level 0.01(2 tailed).

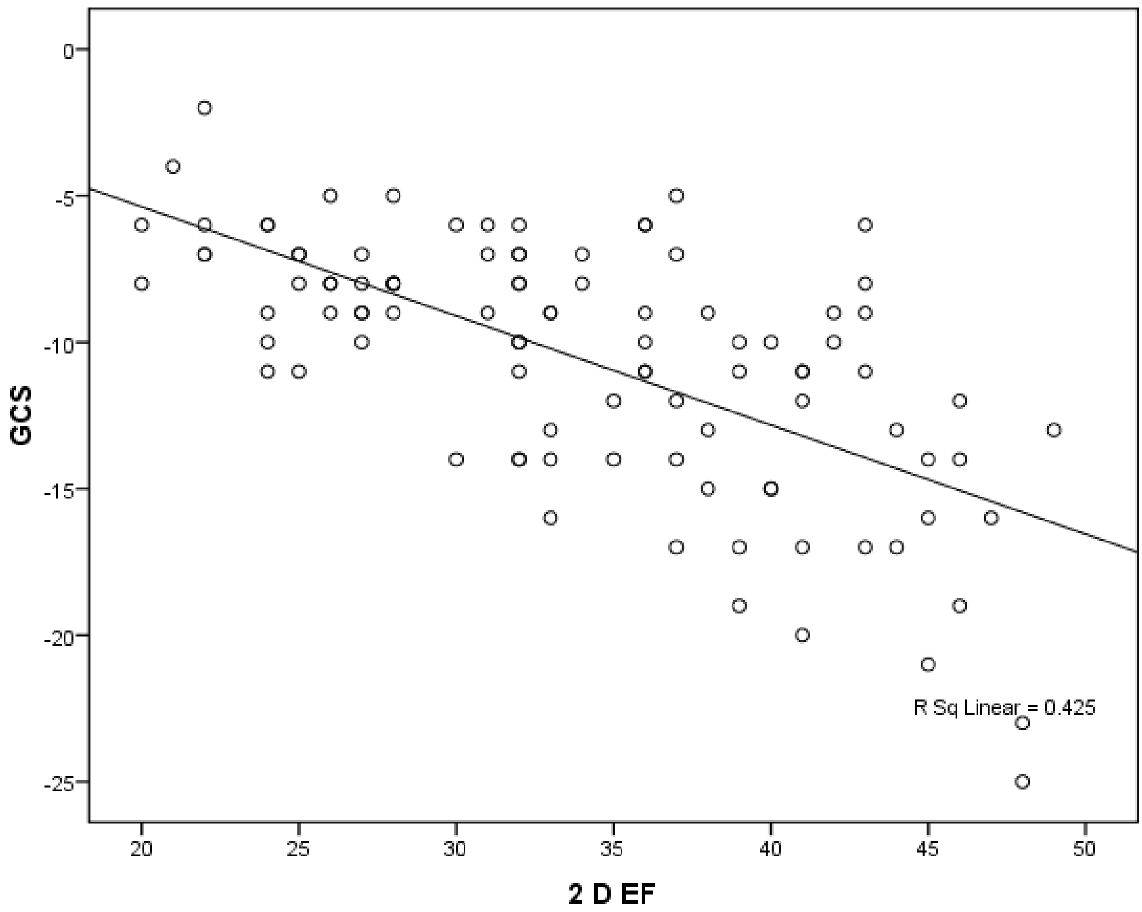

Figure-26: Scatter diagram showing co-relation between 2D EF and GCS.

Co-relation between GCS and 3D EF:

Correlation between 3D EF and GCS was strong and Pearson correlation coefficient r, was 0.632. It was significant at the level 0.01(2 tailed).

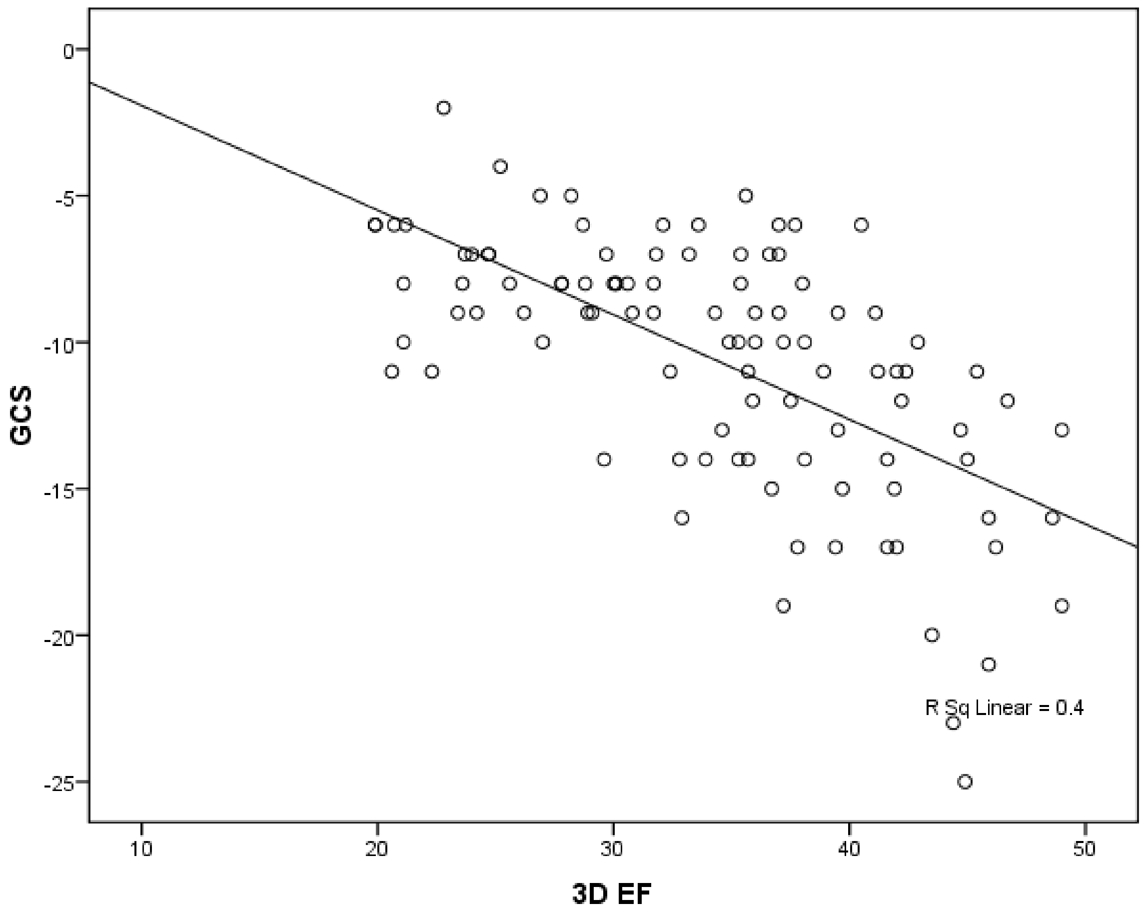

Figure-27: Scatter diagram showing co-relation between 3D EF and GCS.

Co-relation between GLS and 3D EF:

Correlation between 3D EF and GLS was strong and Pearson correlation coefficient r, was 0.717. It was significant at the level 0.01(2 tailed).

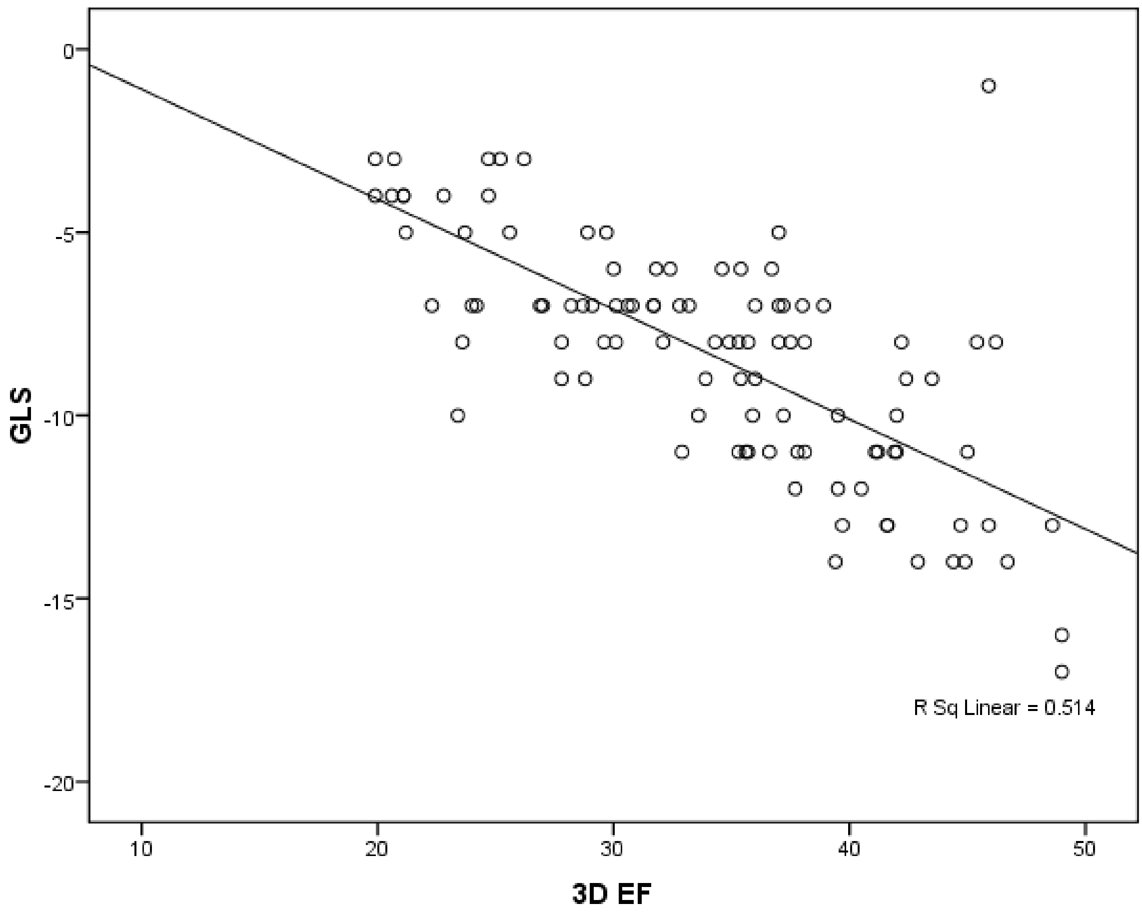

Figure-28: Scatter diagram showing co-relation between 3D EF and GLS.

So the strongest 2D speckle tracking echocardiography co-relate for 2D EF was GLS (r-0.724,P value < 0.01) and for 3D EF was GLS (r-0.717,P value < 0.01).

Co-relation between Global strain with subgroups of LV 2DEF:

Subgroup analysis was done using three categories of 2D EF into less than 30%, between 30% to 40% and 40 to 50%. It demonstrated better co-relation at lower LVEF. Co-relations were improved significantly when 2D EF was low.

Table-4: Correlation between Global strains and various subgroups of LVEF.

Variable	GLS		GCS	
	r	P value	r	P value
Less than 30% (n-31)	-0.36	0.09	-0.75	0.03
30%-39% (n-43)	-0.67	0.015	-0.62	0.02
40%-50% (n-26)	-0.25	0.009	-0.59	0.006

r- Pearson coefficient, n-number of cases

Co-relation between Global strain with subgroups of LV 3DEF:

Subgroup analysis was done using three categories of 3D EF also. It demonstrated better co-relation at lower LVEF. Co-relations were improved significantly when 3D EF was low.

Table-4: Correlation between Global strains and various subgroups of LVEF.

Variable	GLS		GCS	
	r	P value	r	P value
Less than 30% (n-30)	-0.32	0.071	-0.628	0.02
30%-40% (n-46)	-0.76	0.013	-0.720	0.01
40%-50% (n-24)	-0.26	0.009	-0.55	0.007

r- Pearson coefficient, n-number of cases

Inter-observer and intra-observer variation: This study showed that there is good reproducibility for 3D EF in terms of intra-observer and inter-observer variability as intra-class coefficient (ICC) was 0.96 with confidence interval (CI) of 0.85-0.98 for intra-observer and ICC of 0.94 with CI of 0.86-0.98 for inter-observer variation. The very low intra-observer variability for GLS (ICC- 0.99, CI-0.96-0.99, SEM-0.8, COV-0.27) and GCS (ICC-0.99, CI-0.97-0.99, SEM- 0.8, COV 0.25) and low inter-observer variability for GLS (ICC-0.69-0.98, SEM-0.9, COV-0.46) and GCS (ICC-0.99, CI-0.85, SEM-1.0, COV-0.43) that 2D STE derived strains are highly reproducible and accurate.

Table No.-5 Intra-observer variation for GLS, GRS and 3D EF.

Variable	ICC (CI-95%)	SEM	COV
GLS	0.99(0.96-0.99)	0.8	0.27
GCS	0.99(0.97-0.99)	0.8	0.25
3D ejection fraction	0.96(0.85-0.98)	1.0	0.43

ICC-intra-class correlation coefficient

COV-Coefficient of variation

CI-Confidence interval

SEM-Standard error of mean

Table No.-6 Inter-observer variation for GLS, GCS and 3D EF

Variable	ICC (95% CI)	SEM	COV
GLS	0.95(0.66-0.99)	0.9	0.46
GCS	0.97(0.86-0.99)	1.0	0.41
3D EF	0.97(0.86-0.98)	2.6	0.56

ICC-intra-class correlation coefficient

COV-Coefficient of variation

CI-Confidence interval

SEM-Standard error of mean

DISCUSSION

Accurate quantification of LV function has important implication in clinical decision making in various cardiac disease. Two dimensional left ventricular ejection fraction has been the most important prognostic marker in patients with LV systolic dysfunction for a long time. But it has some limitations like image quality, geometric assumptions, subjective interpretation and limited reproducibility.

Current advances in the field of 3D echocardiography have allowed us to calculate LV EF which can overcome some limitations like geometric assumptions and limited reproducibility.

So, this study was planned to see whether global strain acquired by 2D speckle tracking echocardiography was as accurate as 3D ejection fraction. We used 3D ejection fraction as gold standard in this study because already many studies have shown that 3D ejection fraction is comparable to cardiac magnetic resonance imaging acquired ejection fraction(5).

The present study was a prospective observational study which enrolled 100 patients with LV systolic dysfunction. Mean age group was 50 ± 12.4years. Most of patients recruited into study were males (3:1). Out of 100, only 50 patients had undergone coronary angiogram and most of them had CAD.

As we only included patients with LV systolic function and exclude patients with normal LV function. So, the other confounding factors which can affect global strain values in patients with normal LV systolic function like age(51), hypertension(52), diabetics(53), smoker(54), dyslipidemia(55), and chronic kidney disease(56).

This study demonstrated strong co-relation between 2D STE derived global strains and LVEF as calculated by 3D. The same thing has been proven in earlier studies(7). Both GLS (r-0.717, P value < 0.01) and GCS(r-0.632, P value < 0.01) co-relation was good with 3D LV ejection fraction. But, 2D GLS has stronger co-relation with 3D EF as compared to 2D GCS. Earlier study also has proven that(7). But in same study, they have shown that 3D STE derived GCS is better co-related with 3D EF(7). Possible explanation for this is that circumferential fibres are more predominant over longitudinal fibres in myocardium, as proven in histological studies (57).

This study also demonstrated that there is good co-relation between 2D STE derived GLS (r-0.724, P value <0.01) and GCS (r-0.652, P value < 0.01). Same study(7) also has shown that.

This study has validated the feasibility and accuracy of 2D STE assessment of LV function across a wide range of LV ejection fraction. Among the various subgroups of LVEF as calculated by 3D, stronger co-relation was there when EF was less than 40%. This finding also co-related well with earlier studies(7).

This study has shown that there is very less intra-observer variability (ICC-0.96, CI-0.97-0.98, SEM-2.4 and COV-0.27) and inter-observer variability (ICC-0.98, CI-0.96-0.98, SEM-2.6, COV-0.52) in calculating 3D ejection fraction. So, 3D ejection fraction is reproducible and accurate for assessment of LV function. This also co-related with earlier studies(58).

The very low intra-observer variability for GLS (ICC- 0.99, CI-0.96-0.99, SEM-0.8, COV-0.27) and GCS (ICC-0.99, CI-0.97-0.99, SEM- 0.8, COV 0.25) and low inter-observer variability for GLS (ICC-0.69-0.98, SEM-0.9, COV-0.46) and GCS (ICC-0.99, CI-0.85, SEM-1.0, COV-0.43) that 2D STE derived strains are highly reproducible and accurate. The low inter-observer and intra-observer variability makes it a robust marker of LV function with wide spread clinical use. It can replace the conventional 2D biplane Simpson's method. These results also in accordance with the earlier study.

LIMITAIONS

1) Two dimensional speckle tracking echocardiography cannot be used in arrhythmias specifically atrial fibrillation and multiple ventricular ectopics. These make speckle tracking echocardiographic assessment as unreliable because of beat to beat variability.

2) 2D STE is difficult to do if the image sector does not fit into the frame – this could be a problem in very much dilated ventricle.

3) We used 3D EF as a gold standard which has it's own limitations related to the need for good quality image, number of cycles, and patient to hold breath for acquisition.

4) We also did not use the current gold standard for EF, namely the cardiac MRI due to cost and time. (59).

5) As this was prospective observational study, so further independent testing to be done to confirmits predictive value.

CONCLUSION

Our study showed that two dimensional speckle tracking echocardiography derived global strain which is a new modality to assess LV function has good correlation with various groups of LVEF as measured by 2D and 3D. It has less intra-observer and inter-observer variability. Hence 2D STE can be used as yet another parameter to assess LV function.

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ABBREVIATIONS

CAD: CORONARY ARTERY DISEASE

3D: THREE DIMENSIONMAL

2D: TWODIMENSIONAL

GLS: GLOBAL LONGITUDINAL STRAIN

GCS: GLOBAL CIRCUMFERENTIAL STRAIN

MRI: MYOCARDIAL RESONANCE IMAGING

STE: SPECKLE TRACKING ECHOCARDIOGRAPHY

STEMI: ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

LV: LEFT VENTRICLE

EF: EJECTION FRACTION

ABBREVIATIONS FOR MASTER CHART

H NO.- HOSPITAL NMBER

HT- HEIGHT

AG- AGE

SE-SEX

BSA-BODY SURFACE AREA

D-DIAGNOSIS, 1-ISCHEMIC, 2-NON ISCHEMIC

C- COROANRY ANGIOGRAM, 1-NOT DONE, 2-NORMAL, 3-SVD,4-DVD, 5-TVD/LM

H- HYPERTENSION, 1-YES, 2-NO

DM- DIABETES MELLITUS 1- YES, 2-NO

SM- SMOKER 1-YES, 2-NO

DL-DYSLIPIDEMIA 1-YES, 2-NO

HM- HISTORY OF MI- 1-YES, 2-NO

HR-HEART RATE

LVD- LVIDd

LVS- LVIDS

IVD- IVSd

LA- LEFT ATRIUM SIZE

2DE- 2D EF

ESV- END SYSTOLIC VOLUME

EDV- END DIASTOLIC VOLUME

GL4- GLS IN 4 CHAMBER

GL3- GLS IN 3 CHAMBER

GL2- GLS IN 2 CHAMBER

GCB- GCS AT BASE

GCM- GCS AT MID

GCA- GCS AT APEX

IEO- INTEROBSERVER

IAO-INRTRAOBSERVER

j

INFORMED CONSENT

Department of Cardiology
Christian Medical College
Vellore

Use of 2 D speckle tracking Echocardiography for Quantitative Assessment of Global Left Ventricular Function in comparison to 2 D ejection fraction and 3 D ejection fraction

Information sheet

You are being requested to participate in above study.

What is echocardiography?
It is a machine which uses ultrasonic rays to detect any abnormality in heart. Ultrasonic rays are harmless to human body.

If you take part what will you have to do?
If you agree to participate in this study, we will do echocardiography (Ultrasonography of heart) .No additional procedures or blood tests will be conducted for this study.

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

Are there any chances of developing any study related injury?
As we are not using any medicines on you, we do not expect any injury to happen to you.

Will you have to pay for the study investigations?
No extra cost would be charged for the investigations conducted as a part of the study.

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

If you have any further questions, please ask Dr. Parveen Kumar (Mob: 9578487774) or email:drparveenkumar80@gmail.com

C0NSENT FORM

Study Title: Use of 2 D speckle tracking Echocardiography for Quantitative Assessment of Global Left Ventricular Function in comparison to 2 D ejection fraction and 3 D ejection fraction

Study Number:
Participant's name:
Date of Birth / Age (in years):

I____
___________, son/daughter of ___________________________________

(Please tick boxes)
Declare that I have read the information sheet provide to me regarding this study and have clarified any doubts that I had. [ ]

I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]

I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access[]

I understand that my identity will not be revealed in any information released to third parties or published [ ]

I voluntarily agree to take part in this study [ ]

Name:
Signature/Left thumb impression:
Date:

Name of witness:
Signature/Left thumb impression:
Relation to participant:
Date:
Address:

Signature of principle investigator:

PROFORMA

STUDY: Use of 2 D speckle tracking Echocardiography for Quantitative Assessment of Global Left Ventricular Function in comparison to 2 D ejection fraction and 3 D ejection fraction

PATIENT DETAILS:

NAME:

HOSPITAL NO.:

AGE:

SEX:

HEIGHT : cm WEIGHT: kg BSA:

DIAGNOSIS

ANGIO DONE: YES/NO IF YES: 1VD/2VD/3VD/LM

HYPERTENSION:Y/N

SMOKER: Y/N

DIABETES MELLITUS TYPE 2:Y/N

DYSLIPIDEMIA:Y/N

PAST MYOCARDIAL INFARCTION:Y/N

ECHOCARDIOGRAPHIC FEATURES:

HEART RATE:

LVIDd: mm LVIDs: mm IVS: mm PW: mm LA: mm

2D EF:

3D EF: EDV: ESV:

2D LS: AP4: ALAX: AP2: GLS

2D CS: PSAX B: PSAX M: PSAX A: GCS

Hosp.No	AGE	SEX	HT	WT	BSA	D	C	H	SM	DM	DL	HM	HR	LVD	LVS	IVD	PWd	LA	2EF	3DEF	EDV	ESV	GL4	GL3	GL2	GLS	GCB	GCM	GCA	GCS
014192G	48	1	161	54	1.6	1	4	1	2	1	2	1	78	46	41	10	10	36	36	36	90.7	58	-7	-8	-11	-9	-9	-12	-6	-9
834900F	24	1	170	50	1.6	2	1	2	2	2	2	2	88	52	43	12	11	32	48	44.9	109	60.2	-14	-13	-15	-14	-26	-29	-20	-25
016089G	59	1	168	68	1.8	1	1	2	2	2	1	2	59	53	41	11	13	30	48	44.4	74.5	41.4	-17	-13	-13	-14	-20	-20	-29	-23
575448B	60	1	159	54	1.5	2	2	2	2	2	2	2	88	56	51	12	10	46	31	33.6	170	113	-10	-11	-9	-10	-10	-7	-1	-6
015656G	57	1	158	54	1.5	1	4	2	1	1	2	1	79	63	53	10	6	31	28	30.1	114	79.8	-9	-5	-8	-7	-9	-7	-8	-8
020820G	42	2	145	45	1.3	2	1	2	2	1	2	2	105	61	56	7	6	37	22	20.7	101	80.4	-5	-2	-4	-3	-9	-5	-4	-6
752562d	58	1	168	67	1.8	2	1	2	2	2	2	2	65	52	39	9	9	32	46	49	105	53	-19	-14	-19	-17	-15	-21	-22	-19
021179G	50	1	162	50	1.5	2	2	2	2	2	2	2	72	51	42	10	10	31	31	31.7	83.7	57.2	-8	-6	-7	-7	-12	-7	-8	-9
511304F	18	2	158	41	1.4	2	2	2	2	2	2	2	77	58	48	9	9	18	33	33.9	139	92	-9	-9	-8	-9	-15	-17	-9	-14
910362F	32	1	160	69	1.7	2	1	2	1	2	2	2	134	56	47	5	6	46	34	37	95.1	59.9	-5	-5	-7	-5	-7	-10	-2	-7
119087A	44	1	160	69	1.7	1	3	1	2	2	2	2	96	55	43	9	7	26	43	45.4	90.6	49.5	-11	-6	-7	-8	-11	-13	-9	-11
772074F	44	2	158	41	1.4	2	2	1	2	2	2	2	105	51	43	12	11	43	22	24.7	79.2	59.6	-2	-5	-3	-3	-7	-7	-7	-7
743100D	53	1	162	50	1.5	1	4	2	2	1	2	2	75	47	38	11	7	29	32	35.7	73.6	47.3	-9	-14	-10	-11	-15	-15	-13	-14
024399G	38	1	161	54	1.6	2	2	2	2	2	2	2	92	46	37	14	14	49	38	36.7	97.6	61.8	-7	-6	-5	-6	-14	-15	-15	-15
015947G	57	2	156	50	1.5	2	1	2	2	2	2	2	91	64	52	9	10	37	36	37	144	90.3	-9	-6	-6	-7	-7	-6	-3	-6
410644F	52	1	168	67	1.8	1	3	2	2	1	2	2	102	65	52	9	10	38	36	38.9	143	87	-8	-6	-6	-7	-11	-10	12	-11
854426D	51	1	165	56	1.6	1	3	1	2	1	1	2	80	58	48	9	9	42	33	32.9	117	78.7	-11	-11	-11	-11	-18	-16	-15	-16
019784G	38	1	168	62	1.7	2	1	2	2	1	2	2	90	50	40	13	13	42	41	41.6	138	80.8	-12	-14	-13	-13	-18	-17	-16	-17
912784F	33	1	168	75	1.9	1	3	2	1	2	1	1	64	51	42	13	10	33	40	41.9	114	47.9	-12	-8	-13	-11	-18	-10	-25	-15
915801F	45	2	154	63	1.6	2	2	1	2	1	2	2	116	53	45	10	13	37	32	36	112	71.5	-8	-7	-7	-7	-13	-9	-9	-10
922668F	46	2	160	64	1.7	2	1	2	2	2	2	2	76	48	38	10	10	32	42	42.9	55.7	31.8	-14	-16	-11	-14	-10	-12	-9	-10
025937G	54	1	162	65	1.7	1	5	2	2	1	1	2	95	56	49	11	12	53	24	20.6	123	97.4	-4	-5	-4	-4	-6	-14	-12	-11
026160G	50	1	172	74	1.9	1	1	1	1	2	2	2	73	56	36	12	10	33	37	35.6	127	81.6	-15	-7	-10	-11	-8	-10	-2	-5
368193D	65	1	159	54	1.5	1	1	1	2	1	1	2	98	62	56	11	9	33	27	27.8	91.6	66.1	-9	-9	-9	-9	-9	-6	-9	-8
765185D	67	2	155	46	1.4	2	1	1	2	2	2	2	81	63	56	8	10	45	24	23.4	163	125	-10	-9	-9	-10	-11	-9	-6	-9
705499F	48	1	158	58	1.6	2	2	2	1	1	2	2	128	65	58	8	8	50	21	25.2	132	98.4	-2	-3	-4	-3	-10	-2	1	-4
915696F	56	2	155	52	1.5	2	2	2	2	1	1	2	105	70	64	5	10	46	25	24.7	204	154	-4	-5	-2	-4	-2	-4	-18	-7
026667G	61	1	163	62	1.7	1	1	2	2	2	2	2	72	62	51	10	11	37	27	31.8	152	103	-5	-7	-5	-6	-9	-5	-7	-7
917138	47	1	165	65	1.7	1	1	1	1	2	2	2	85	47	37	10	10	29	43	40.5	76	46	-13	-12	-11	-12	-5	-7	-7	-6
694039A	57	1	172	70	1.8	1	4	1	2	2	2	2	82	53	43	7	7	37	32	36.6	89.5	56.7	-8	-11	-14	-11	-10	-3	-5	-7
025412g	53	1	164	46	1.5	1	5	1	2	1	2	2	96	70	64	11	9	45	20	21.1	171	135	-7	-5	-2	-4	-11	-6	-6	-8
027019G	51	1	168	61	1.7	2	1	2	2	2	2	2	66	69	61	12	14	57	26	28.2	227	163	-7	-8	-5	-7	-4	-7	-4	-5

Hosp.No	AGE	SEX	HT	WT	BSA	D	C	H	SM	DM	DL	HM	HR	LVD	LVS	IVD	PWd	LA	2EF	3DEF	EDV	ESV	GL4	GL3	GL2	GLS	GCB	GCM	GCA	GCS
917177F	33	1	169	52	1.7	1	1	2	2	2	2	2	89	47	38	9	6	28	40	38.1	84.4	52.2	-12	-11	-10	-11	-11	-13	-6	-10
031352G	57	2	156	50	1.5	2	1	1	2	2	2	2	73	61	51	12	11	37	22	22.8	137	106	-4	-4	-4	-4	-3	-2	-2	-2
326849F	48	1	157	68	1.7	1	5	1	1	2	2	1	69	67	61	7	7	34	33	30.8	121	80	-8	-5	-8	-7	-9	-8	-11	-9
917334F	50	1	150	45	1.4	1	1	1	1	1	2	1	94	45	35	8	7	27	43	38	97.5	60.4	-6	-5	-9	-7	-9	-10	-6	-8
917097F	60	1	150	44	1.4	1	1	2	2	2	2	2	79	45	36	7	8	22	39	37.2	87.7	55.1	-8	-8	-6	-7	-16	-10	-6	-10
024075G	46	2	158	48	1.5	1	1	2	2	2	2	1	72	57	43	9	11	44	44	46.2	145	78.1	-8	-10	-7	-8	-20	-14	-17	-17
026191G	61	1	166	59	1.7	1	5	2	1	1	2	1	70	51	43	13	7	37	49	49	92.6	45.3	-18	-15	-14	-16	-16	-16	-14	-13
032451G	45	1	161	55	1.6	1	3	2	1	2	1	1	83	61	53	8	10	41	26	26.2	144	106	-4	-2	-5	-3	-13	-7	-5	-9
904478F	23	2	148	46	1.4	2	1	2	2	2	2	2	109	57	52	10	10	39	24	19.9	121	97.2	-4	-3	-3	-3	-7	-5	-6	-6
010139G	60	2	151	38	1.3	2	1	2	2	2	2	2	81	59	49	8	11	41	32	33.2	140	93.8	-6	-8	-9	-7	-9	-6	-5	-7
374588C	55	2	158	48	1.5	2	2	2	2	2	2	2	71	63	54	6	6	39	32	28.8	187	133	-7	-8	-13	-9	-12	-7	-6	-8
917923F	43	1	165	45	1.5	2	1	1	2	1	2	2	116	53	46	13	12	41	30	29.6	118	82.9	-8	-7	-9	-8	-15	-15	-11	-14
917741F	54	1	158	54	1.5	1	4	2	1	1	2	2	65	46	35	13	8	43	47	48.6	88.4	45.4	-14	-12	-12	-13	-17	-16	-16	-16
917609F	63	2	154	63	1.6	1	5	2	2	2	1	2	69	47	42	8	10	31	41	43.5	101	56.9	-10	-11	-7	-9	-10	-22	-27	-20
033572G	60	2	145	52	1.4	1	4	2	2	1	2	2	98	56	48	11	10	37	30	28.7	160	114	-6	-6	-9	-7	-5	-6	-5	-6
840867F	52	1	165	65	1.7	1	3	2	1	2	2	1	67	52	41	8	11	39	41	42.2	132	76.3	-8	-8	-9	-8	-16	-12	-9	-12
032253G	19	2	146	40	1.3	2	1	1	2	2	2	2	110	49	44	16	13	38	25	22.3	111	85.9	-6	-5	-8	-7	-14	-13	-4	-11
973080C	60	1	172	72	1.9	2	1	1	2	2	1	1	101	61	53	8	10	39	28	26.9	273	200	-7	-10	-6	-7	-3	-4	-8	-5
917859F	41	2	154	48	1.4	2	1	2	2	1	2	2	83	51	44	11	10	37	26	27.8	99	71.4	-8	-7	-8	-8	-14	-7	-5	-8
042896G	71	1	175	74	1.9	1	1	2	2	1	2	2	102	55	42	12	9	35	27	24.2	184	139	-7	-5	-8	-7	-9	-8	-9	-9
809021F	54	1	170	75	1.9	2	2	2	2	2	2	2	82	67	56	11	9	43	28	30.6	108	74.8	-8	-5	-9	-7	-5	-5	-10	-8
917867F	50	1	165	55	1.6	2	1	1	2	1	2	2	113	45	36	8	7	22	39	37.2	87.7	55.1	-9	-12	-8	-10	-9	-21	-28	-19
800654F	42	1	165	54	1.6	1	1	2	1	2	2	1	84	62	52	9	11	40	24	21.2	106	83.2	-5	-5	-5	-5	-6	-6	-4	-6
042491G	72	1	162	54	1.6	2	1	2	1	2	2	2	105	71	63	12	13	42	27	27	212	155	-6	-9	-6	-7	-14	-8	-8	-10
043858G	61	2	145	41	1.3	2	1	2	2	2	2	2	87	62	51	10	11	32	28	29.1	142	101	-6	-7	-7	-7	-7	-7	-12	-9
033614G	52	1	160	60	1.6	1	4	2	1	1	2	1	67	47	37	15	13	39	46	45	84	46.3	-10	-9	-14	-11	-14	-17	-11	-14
781438F	54	1	164	68	1.7	1	4	1	1	1	2	1	76	56	44	9	10	35	37	37.8	94.4	45.4	-11	-8	-9	-11	-22	-16	-16	-17
917476F	74	1	164	68	1.7	2	1	2	2	1	2	2	107	60	44	8	9	33	28	30.1	103	71.7	-7	-7	-8	-8	-8	-9	-5	-8
794312f	46	1	168	75	1.9	2	2	2	2	2	2	2	67	58	47	10	10	39	36	35.7	92.3	59.3	-8	-9	-7	-8	-10	-8	-22	-11
786505B	67	2	152	56	1.5	1	1	2	2	2	2	1	100	54	44	8	10	41	32	34.9	138	89.7	-8	-9	-7	-8	-12	-6	-13	-10
044216G	61	1	176	78	1.9	1	5	2	2	2	2	1	90	66	59	12	10	47	25	24	150	114	-8	-7	-5	-7	-11	-4	-4	-7
040255G	69	1	170	74	1.9	1	5	2	2	2	2	1	84	57	46	11	11	37	34	35.4	135	86.9	-9	-10	-10	-9	-6	-11	-6	-8

Hosp.No	AGE	SEX	HT	WT	BSA	D	C	H	SM	DM	DL	HM	HR	LVD	LVS	IVD	PWd	LA	2EF	3DEF	EDV	ESV	GL4	GL3	GL2	GLS	GCB	GCM	GCA	GCS
920435F	70	1	165	55	1.6	1	3	2	1	2	2	2	72	51	41	11	7	33	35	35.3	143	93	-12	-10	-11	-11	-18	-11	-12	-14
898715F	36	1	172	68	1.8	1	3	2	1	2	2	2	69	40	30	11	6	27	45	45.9	101	54.4	-14	-13	-12	-13	-13	-15	-20	-16
037967G	29	1	178	85	2	1	1	2	2	1	2	2	101	56	45	11	11	45	28	31.7	140	94.9	-6	-7	-8	-7	-7	-9	-9	-8
042786G	51	1	175	74	1.9	1	1	1	1	2	2	1	91	52	42	13	11	37	40	39.7	117	70.6	-12	-13	-15	-13	-11	-12	-22	-15
032233G	64	2	152	38	1.3	1	5	2	2	2	1	2	81	49	38	6	6	30	45	45.9	101	54.4	-18	-15	-14	-1	-19	-15	-33	-21
044335G	55	1	165	68	1.8	1	1	1	1	1	2	1	120	62	57	11	11	43	20	19.9	143	114	-3	-5	-3	-4	-9	-6	-4	-6
029657G	68	1	170	68	1.8	2	1	2	2	1	2	1	89	55	45	10	10	35	37	38.1	148	91.5	-8	-7	-9	-8	-15	-16	-10	-14
462943D	20	2	160	55	1.6	2	1	1	2	2	2	2	82	59	48	11	8	36	37	37.5	117	72.8	-7	-9	-8	-8	-14	-13	-9	-12
513041C	66	1	162	68	1.7	1	4	2	1	2	1	1	68	50	40	7	12	32	43	39.5	134	81.3	-9	-9	-13	-10	-8	-9	-12	-9
428062	50	1	170	68	1.8	1	3	2	1	2	1	1	106	56	47	11	9	47	32	32.1	101	68.8	-7	-8	-9	-8	-8	-8	-3	-6
033343G	24	1	170	50	1.6	2	2	2	2	2	2	2	112	60	54	11	12	45	22	23.7	156	119	-3	-5	-7	-5	-6	-7	-8	-7
605931	51	1	166	66	1.7	1	1	1	1	1	1	1	107	49	43	14	10	40	31	29.7	101	71.2	-4	-6	-6	-5	-9	-7	-6	-7
048672G	57	2	154	57	1.6	1	1	1	2	1	1	1	93	58	50	11	7	38	24	21.1	112	88	-3	-3	-5	-4	-15	-8	-7	-10
048433G	44	2	158	58	0.2	2	1	1	2	1	2	2	110	52	43	11	10	45	26	23.6	131	99.9	-8	-6	-11	-8	-7	-7	-11	-8
783449D	49	1	168	75	1.9	2	1	2	1	2	2	2	107	61	54	11	13	47	25	25.6	169	126	-6	-3	-5	-5	-8	-9	-8	-8
045899G	59	1	170	60	1.7	1	3	1	1	1	2	1	120	47	39	13	9	30	42	41.1	93.6	55.1	-11	8	-13	-11	-9	-8	-9	-9
915380F	51	1	166	56	1.6	1	1	1	1	1	2	1	101	47	40	10	11	32	27	28.9	76.8	54.7	-5	-6	-5	-5	-12	-6	-10	-9
845387C	66	1	172	72	1.9	1	4	1	2	1	2	1	59	58	45	16	11	39	39	41.2	99	58.2	-11	-12	-10	-11	-10	-9	-13	-11
047780G	69	1	162	68	1.7	1	4	2	1	2	2	1	61	51	42	12	11	36	35	35.9	128	82.1	-10	-10	-9	-10	-13	-14	-10	-12
051637G	63	1	165	55	1.6	1	1	2	1	1	2	1	91	56	51	9	8	40	32	32.4	123	83.3	-6	-5	-7	-6	-17	-12	-6	-11
788420F	46	1	165	62	1.7	1	4	2	1	1	2	1	78	58	46	7	9	35	45	41.6	115	67.1	-12	-13	-14	-13	-15	-17	-11	-14
378324D	46	1	188	77	2	2	2	1	1	1	2	2	96	61	48	13	12	40	36	35.3	124	80.1	-9	-7	-10	-8	-10	-10	-9	-10
208131D	49	1	161	53	1.6	1	3	1	2	1	1	1	79	51	44	7	10	42	32	32.8	103	69.1	-6	-7	-7	-7	-18	-12	-12	-14
048814G	67	1	174	78	1.9	1	5	1	2	1	2	1	55	57	48	11	11	46	33	34.3	137	89.9	-8	-9	-8	-8	-13	-8	-4	-9
053493G	53	1	170	78	1.9	1	4	2	2	1	1	2	94	69	57	7	10	43	36	37.7	168	105	-10	-12	-13	-12	-8	-4	-6	-6
686710F	41	1	155	47	1.4	2	1	2	2	2	2	2	68	58	46	10	10	41	39	39.4	153	92.8	-15	-15	-13	-14	-16	-16	-19	-17
202671F	55	1	168	74	1.8	1	3	2	2	1	1	1	78	65	53	9	11	33	37	35.4	134	86.7	-6	-8	-5	-6	-10	-6	-6	-7
051465G	39	1	170	80	1.9	1	4	1	2	1	2	1	79	46	36	13	11	36	44	44.7	91.1	50	-15	-14	-13	-13	-17	-3	-25	-13
738853d	42	2	160	67	1.7	2	1	1	2	2	2	2	88	55	42	9	10	40	41	42.4	120	69.2	-14	-9	-5	-9	-9	-13	-13	-11
240888B	41	2	152	48	1.4	2	1	2	2	1	1	2	70	50	38	12	11	34	38	39.5	99.4	60	-12	-11	-13	-12	-8	-15	-16	-13
920120F	42	1	168	64	1.7	1	3	1	2	1	2	2	106	64	51	11	12	47	38	37	176	111	-9	-7	-7	-8	-7	-9	-11	-9
055341G	45	1	168	62	1.7	2	1	2	1	2	2	2	81	65	51	12	13	51	41	42	161	93.3	-10	-10	-10	-10	-13	-12	-9	-11

406520C	44	1	174	80	2	2	1	2	2	2	2	2	103	71	60	12	12	40	32	30	228	160	-7	-5	-6	-6	-9	-8	-8	-8
213875B	46	1	170	75	1.9	1	5	1	2	1	2	2	74	56	43	10	10	33	46	46.7	110	58.4	-13	-14	-14	-14	-2	-15	-16	-12
918744F	23	1	151	52	1.5	2	1	1	2	2	2	2	83	59	45	16	15	41	43	42	157	91.1	-12	-10	-10	-11	-18	-16	-7	-17
710872C	41	1	165	65	1.7	2	1	1	2	2	2	2	70	61	51	13	13	42	33	34.6	145	94.8	-6	-6	-7	-6	-18	-9	-11	-13
IAO																														
014192G													80	46	38	10	10	36	31	37.3	94	58.3	-8	-7	-10	-8	-8	-11	-7	-9
015656G													76	63	53	10	6	31	27	29.5	111	78.4	-10	-5	-8	-7	-8	-7	-6	-7
024399G													98	46	37	14	14	49	40	37.6	104	65.3	-8	-7	-5	-7	-13	-14	-15	-14
883479F													76	46	38	10	10	32	41	42.5	57.8	33.3	-13	-15	-13	-14	-10	-10	-8	-9
694039A													82	53	43	7	7	37	34	35.8	88.4	56.8	-9	-13	-12	-11	-8	-5	-9	-7
032253G													112	49	44	16	13	38	24	23.1	108	83.4	-6	-4	-7	6	-12	-14	-4	-10
809021F													88	67	56	11	9	43	29	31.2	101	69.8	-6	-5	-10	-7	-5	-5	-10	-8
917476F													100	60	44	8	9	33	27	29.5	98.5	69.5	-7	-6	-8	-7	-8	-8	-5	-7
037967G													96	56	45	11	11	45	28	31.5	136	93.3	-6	-8	-7	-7	-7	-8	-10	-8
044335G													112	62	57	11	11	43	19	19.5	149	120	-4	-5	-3	-4	-9	-6	-4	-6
IEO																														
575448B													88	56	51	12	10	46	31	32.9	168	113	-9	-1	-9	-10	-10	-8	-1	-6
836900F													88	52	43	12	11	32	47	44.4	105	58.6	-14	-12	-15	-14	-28	-30	-18	-25
910362F													134	56	47	5	6	46	35	37.4	100	62.6	-5	-6	-6	-5	-7	-8	-4	-7
915801F													116	53	45	10	13	37	33	35.2	113	73.5	-8	-6	-6	-6	-14	-8	-9	-10
462943D													83	59	48	11	8	36	39	36.8	114	72.3	-7	-10	-6	-8	-15	-13	-8	-12
428062													106	56	47	11	9	47	33	31.5	100	68.7	-7	-6	-9	-7	-7	-8	-3	-6
032233G													81	49	38	6	6	30	46	46	102	55.3	-18	-14	-15	-16	-18	-15	-31	-21
781438F													76	56	44	9	10	35	37	36.5	95.6	60.7	-9	-10	-9	-9	-11	-22	-16	-15
917859F													83	51	44	11	10	37	27	27.2	100	72.8	-8	-6	-8	-8	-14	-6	-5	-8
840867F													67	52	41	8	11	39	40	43.5	136	76.8	-8	-8	-9	-8	-15	-12	-9	-12