ASSESSMENT OF LV SYSTOLIC FUNCTION BY VELOCITY VECTOR IMAGING

A DISSERTATION
SUBMITTED IN PARTIAL FULFILLMENT
OF DM – BRANCH II CARDIOLOGY EXAMINATION
OF THE TAMILNADU DR. MGR MEDICAL
UNIVERSITY, CHENNAI, TO BE HELD IN
JULY/AUGUST 2008.

CERTIFICATE

This is to certify that the thesis titled **"Assessment of LV systolic function by velocity vector imaging"** is the bonafide work of the candidate **Dr.Kumar.N,** towards partial fulfillment of DM - Branch II (Cardiology) Examination of the Tamilnadu Dr. MGR Medical University, Chennai, to be conducted in July/August 2008.

Dr. George Joseph, MD DM (CARD)
Professor & Head,
Department of Cardiology,
Christian Medical College,
Vellore – 632 004.

CERTIFICATE

This is to certify that the thesis titled **"Assessment of LV systolic function by velocity vector imaging"** is the bonafide work of the candidate **Dr.Kumar N,** towards partial fulfillment of DM - Branch II (Cardiology) Examination of the Tamilnadu Dr. MGR Medical University, Chennai, to be conducted in July / August 2008.

Guides:

Dr. Paul V George, MD DM (CARD)
Professor & Ag. Head
Department of Cardiology Unit II,
Christian Medical College,
Vellore – 632 004.

Dr. V. Jacob Jose, MD DM (CARD) FACC, MS, FCCP, FIAE
Professor
Department of Cardiology,
Christian Medical College,
Vellore – 632 004.

ACKNOWLEDGEMENTS

The DM thesis was a challenging but valuable learning experience. I thank God for helping me to finish it successfully. All along, there have been people who helped me and without whom this thesis would not have been possible.

I am immensely grateful to Professors Dr. V. Jacob Jose and Dr. Paul George who provided guidance, encouragement and support for my thesis at all stages.

I am grateful to Dr. George Joseph, Head of the Department for his encouragement and support.

I am thankful to Dr Sunil Chandy, Dr. Oommen George and the entire faculty in the department who have provided a conducive and academic environment in which to carry out the dissertation.

I thank Dr. Regi Oommen, Professor of Nuclear Medicine for facilitating smooth performance and analysis of gated SPECT.

I would also like to thank my parents for providing moral support and encouragement at all times.

Lastly, I am immensely grateful to all the patients who participated in this study and who always form the epicenter of all our learning.

Dr. Kumar. N.

CONTENTS

Page

Abstract

1. Introduction ---- 1
2. Aims and Objectives ---- 3
3. Review of Literature ---- 4
4. Methodology ---- 42
5. Results ---- 45
6. Discussion ---- 54
7. Limitations ---- 59
8. Summary of Main Findings ---- 60
9. Bibliography ---- 61
10. Appendix:
    - Study Proforma
    - Master Chart
    - Glossary for Master chart

Abstract

ASSESSMENT OF LV SYSTOLIC FUNCTION BY VELOCITY VECTOR IMAGING

BACKGROUND: Assessment of LV systolic function is an important parameter in evaluation of cardiac disease. Echocardiography is the most widely used non invasive imaging modality in the assessment of LV function. Current methods of assessing LV systolic function have limitations. Velocity vector imaging (VVI) is a new modality that uses 2D (B-mode) images to determine tissue motion and velocity by application of a tracking algorithm. In this study, we assessed the utility of VVI in the measurement of LV systolic function in comparison to radionuclide imaging and standard 2D echo.

METHODS: We measured global and regional LV systolic function by ejection fraction (EF) in 49 patients using VVI, standard 2D echo and nuclear imaging (SPECT). Patients were categorized as normal; mild, moderate or severe LV systolic dysfunction based on American Society of Echocardiography classification. The results were analyzed by appropriate statistical tests for correlations.

RESULTS: The mean EF for the study population as measured by VVI was 35 ± 12.08%, as compared to 54.2 ± 19.51% with SPECT ($p<0.001$ vs VVI) and 50.3 ± 8.92% with 2D echo($p<0.001$ vs VVI). There was a positive linear correlation between EF measured by VVI and the other modalities (Pearsons correlation coefficient 0.577 for SPECT and 0.573 for 2D; $p = 0.01$). However, VVI systematically underestimated the EF in comparison to SPECT. There were significantly greater proportion of patients classified as having moderate or severe LV systolic dysfunction by VVI (75.5%) when compared to SPECT (34.7%; $p=0.026$). We derived a correction factor to calculate SPECT EF from VVI EF: EF (SPECT) = EF (VVI) x0.9 + 21 or approximately VVI (EF) +20. There was good inter-observer correlation for EF measured by SPECT.

CONCLUSION: VVI was found to underestimate the ejection fraction as compared to that measured by gated SPECT. A correction factor can be incorporated into the VVI algorithm to improve its accuracy.

INTRODUCTION

Cardiovascular disease is one of the leading causes of morbidity and mortality worldwide. Our country has faced an epidemic of ischemic heart disease over the past decade. Hence new tools for diagnosis and prognostication in heart disease are constantly being developed and evaluated.

Measurement of left ventricular (LV) function has a central role in the assessment of a wide variety of cardiac diseases. While measurement of systolic function is almost always done as a routine, detailed evaluation of diastolic function is done in selected instances. The degree of LV systolic dysfunction is a powerful predictor of cardiovascular morbidity and mortality[1] and is often crucial in deciding therapy. Clinical evaluation alone has been shown to have poor sensitivity and specificity to detect LV dysfunction, while the electrocardiogram and chest X-ray have only limited utility[2]. Though several new tools such as CT and MRI have entered the diagnostic armamentarium, echocardiography continues to be the most important and widely used modality in the measurement of LV systolic function. In this regard, the ejection fraction (EF) has been the most commonly used measure of LV systolic function. With real-time two dimensional imaging of the heart, it has been possible to rapidly and non-invasively measure EF and also perform serial measurements to track the course of disease. EF is a simple and easy to understand numeric measure, and has been shown to predict survival[3]. Though EF has limitations as a true indicator of LV function, it continues to have global appeal[4]. However, a greater problem often is technical difficulties in measurement of EF, especially with respect to correct endocardial border detection which is crucial to the accuracy of measured EF[5]. In the era of revolutionary device therapy for heart failure, accurate measurement of EF has assumed even greater importance than before, as it is a crucial deciding factor in cardiac

resynchronization (CRT) and implantable cardioverter defibrillator (ICD) therapy[6]. Thus it is important to look at ways and means of overcoming technical limitations in measurement of EF by echocardiography.

Speckle tracking echocardiography (STE) is an exciting new tool with promising potential which uses natural acoustic markers in conventional gray scale ultrasound images[7]. This can be potentially used to track motion of the myocardium. A new technology based on speckle tracking is velocity vector imaging (VVI) which displays velocities of the myocardium using a unique and multi-dimensional tracking algorithm[8]. VVI may thus be helpful in accurately tracking endocardial movement and potentially improving measurement of LV volumes and EF. There are no studies systematically assessing the utility of VVI in the assessment of LV systolic function. The present study was hence undertaken to measure ejection fraction with VVI and to compare it with standard two dimensional (2D) echocardiography and nuclear single photon emission computed tomography (SPECT).

AIMS AND OBJECTIVES

Aim:

The aim of the study is to assess the accuracy of the new echocardiographic modality, velocity vector imaging in measuring left ventricular ejection fraction by comparing it with nuclear gated SPECT and standard 2D echo.

Objectives:

1. To measure global and regional EF using velocity vector imaging in a cohort of patients.
2. To find out the correlation between EF measured by VVI and that measured by nuclear gated SPECT and standard 2D echo.
3. To classify patients into categories of LV dysfunction based on EF measured by VVI and compare it with similar categorization done using SPECT and 2D echo.
4. To calculate a correction factor, if needed, for EF measurement by VVI, keeping SPECT as the “gold standard”

REVIEW OF LITERATURE

Echocardiography is an extremely useful and extensively used investigative modality. Its advantages include ease of performance, ready availability, portability and avoidance of intravenous contrast or radiation. The assessment of LV systolic function is a key part of the echocardiographic examination. Various methods are available to measure LV systolic function by echo, though none is perfect. It is being increasingly recognized that left ventricular geometry[9] and motion is complex and multi-dimensional, and a single measure of LV systolic function may not be all-encompassing. Thus, there is a constant endeavour to develop newer echocardiographic techniques to better assess LV performance.

Physiology of Cardiac contraction:

The myocardial muscle cells or myocytes are the cells responsible for executing the contraction-relaxation function of the heart. They constitute a major volume and mass of the myocardium. Groups of myocytes form myofibers. Myocytes are bound by a membrane called the sarcolemma which forms invaginations called T tubules. The major cellular organelle within the myocyte responsible for triggering contraction is the sarcoplasmic reticulum (SR) which has large stores of calcium. A wave of depolarization initially releases a small amount of calcium from the T tubules which then cause a larger release from the SR initiating contraction. Conversely, when the calcium is taken back into the SR, relaxation ensues.
The contractile proteins of the heart are the thin actin and thick myosin filaments. Calcium ions start the contraction process by interacting with troponin C and remove the inhibitory effect of troponin I. Contraction is achieved by sliding of the actin over the myosin filaments. By this, the two ends of the fundamental contracting unit, called the sarcomere are drawn

towards each other, resulting in shortening. Contraction is an energy-dependent process which is achieved by breakdown of adenosine triphosphate (ATP). The opposite process occurs in relaxation. An understanding of the molecular mechanisms involved in contraction-relaxation helps to clarify the role of physiologic and metabolic factors in modulating LV contraction. For example, catecholamines increase LV contractility by acting on β1 adrenergic receptors which cause a cyclic AMP mediated increase of calcium release from the sarcoplasmic reticulum.

The Cardiac Cycle:

Onset of left ventricular contraction caused by depolarization causes a build up of pressure in the LV. When left ventricular (LV) pressure exceeds left atrial pressure, closure of the mitral valve occurs producing the first heart sound. This is followed by isovolumic contraction, during which time pressure in the ventricle rapidly rises. When the LV pressure exceeds aortic pressure, the aortic valve opens and the phase of ejection begins, during which time, the LV volume declines. In the first half of ejection, LV pressure exceeds that of the aorta producing rapid ejection, while in the second half as LV pressure declines, slow ejection is maintained by the elastic recoil of the aorta. The aortic valve closes at the end of ejection producing the second heart sound and diastole starts. As the LV pressure drops below that in the left atrium, the phase of early or rapid filling occurs. Active diastolic relaxation in early diastole creates a suction which aids in rapid filling. As the pressures in the atrium and LV equalize, filling almost stops (diastasis) and then occurs again in late diastole by virtue of the atrial contraction. Normally most filling occurs during the early filling phase. However, atrial contribution becomes important when cardiac output needs to rise as during exercise, or when ventricular relaxation is impaired due to stiffening of the ventricle as in pathological hypertrophy[10]. LV volume is maximal at end diastole and minimal at end systole.

Frank-Starling Mechanism:

Within physiological limits, if a larger heart volume increases the initial length of the muscle fiber, the contraction is stronger and thus more blood would be ejected. The rate of rise of pressure is more rapid and so is the rate of relaxation[11]. This principle is important in changes in cardiac output which occurs in physiological conditions.

Preload refers to the initial ventricular volume or pressure prior to onset of contraction, which would essentially be the state of the ventricle at end-diastole. As evident from the Frank-Starling principle described above, preload is important in determining the strength of the subsequent LV contraction.

Afterload refers to the systolic load on the ventricle once it has started to contract and essentially offers resistance to ventricular ejection. The degree of afterload dictates LV wall stress. In a normal heart, the LV can overcome most acute changes in load. However, if a significant resistance continues over a period of time, compensatory change in the form of hypertrophy would occur to generate additional pressures.

Definitions:

Systole is defined as the portion of the cardiac cycle from mitral valve closure to aortic valve closure.

Stroke volume is the amount of blood ejected from the left ventricle in a single cardiac cycle and the total amount of blood ejected in a minute is the *cardiac output.* Thus the cardiac output equals the product of the stroke volume and the heart rate.

LV systolic function is a measure of the contractility of the left ventricle. This is affected by several factors including heart rate, metabolic factors and drugs. Additionally the preload and the afterload (aortic resistance/impedance) also determine the stroke volume. Increasing preload causes an increase in stroke volume by the Frank-Starling mechanism[11], while an

increase in afterload results in a fall in the stroke volume. Thus, a pure measurement of ventricular contractility independent of loading conditions poses challenges.

Diastolic function refers to the relaxation properties of the LV. Normal diastolic function is also important to the overall function of the heart, as a proper and adequate relaxation determines the preload of the subsequent systole. Hence systolic and diastolic functions are not strictly separate and are in fact intertwined with each other. However, for clinical purposes, they are studied separately using different measures.

Various methods have been developed in echocardiography to measure LV systolic function including M-mode, 2D, Doppler and new techniques such as tissue Doppler imaging, strain and strain rate. In addition, 3D echo has now emerged as a potential tool for accurate LV volume measurement. A brief overview of these methods is given below before discussing the emerging avenues of speckle tracking and velocity vector imaging.

M-MODE:

The early attempts to measure LV function used M-mode echocardiogram to perform linear measurements of the LV. The advantage of M-mode is the superior temporal resolution compared to 2D echo. Measurement of the LV dimensions in end diastole and end systole give an idea of the LV volumes.

Fractional shortening (FS) can be calculated as the difference between the end diastolic and end systolic dimensions of the LV, divided by the end diastolic dimension. Fractional shortening is a rough measurement of LV systolic function; with the measured value being compared to an established normal range [12]. Although simple to measure, FS is dependent on loading conditions and heart rate[13].

The *velocity of circumferential fiber shortening* (Vcf) is obtained by dividing FS by the ejection time and is relatively preload independent[14].

Another linear measurement is the *descent of the base*. During LV contraction, the base of the heart moves toward the apex, and as the apex is relatively fixed; this movement is directly proportional to systolic function. M-mode interrogation of the lateral mitral annulus is done and the amount of excursion determined.

E-point septal separation: The magnitude of opening of the mitral valve, which is seen as the height of the E-wave in an M-mode cut, correlates with transmitral flow and therefore stroke volume. Similarly, the LV internal dimension in diastole correlates with end-diastolic volume. So, a comparison of the above two parameters can give an idea of the ejection fraction. This is obtained by measuring the distance between the mitral valve E point and the left side of the ventricular septum. An increase in this distance reflects a decreased ejection fraction.

Looking at the pattern of aortic valve opening also provides indirect assessment of LV function. If the stroke volume is reduced, there is a gradual reduction of forward flow in late systole, which results in a gradual closure of the aortic valve giving a rounded appearance[15].

Regional function can be assessed by looking at systolic thickening. However, this requires both the endocardium and the epicardium to be defined; the latter posing technical difficulties. 2D guided M-mode imaging in different planes may have to be used for optimal visualization; however normal ranges for quantitative assessment have not been well defined.

M-mode suffers from certain disadvantages. It can underestimate or overestimate the LV function if the M-mode beam is oblique with respect to the long or short axis of the ventricle. Even using 2D guided M-mode; it may not be always possible to align the beam properly. Further, M-mode provides assessment along a single line of interrogation and regional variation in ventricular function is not accounted for. Methods have been developed to calculate volumes and ejection fraction from M-mode measurements such as the Teichholz method and the Quinones method but these suffer from the shortcoming of making inaccurate assumptions about LV cavity shape and size[16]. Increasingly, M-mode is being supplanted by

more direct measures of LV size and function available from two dimensional echocardiography.

TWO DIMENSIONAL ECHOCARDIOGRAPHY:

Two-dimensional echocardiography (2 D echo) gives greater spatial resolution to measure LV function. Determination of LV volumes is based on endocardial border tracing at end-diastole and end-systole in one or more planes. Prerequisites for a good 2D examination include good image quality, adequate endocardial definition and proper visualization of the apex of the LV. A simple 2D measure of LV function is the fractional area change (FAC) which is calculated in the short axis view of the left ventricle by comparing the diastolic area with the systolic area. However, this represents LV function only at the level being interrogated and thus will not reflect regional dysfunction.

Ejection Fraction:

2D echo is used to measure left ventricular volumes and to calculate the ejection fraction (EF) from it. The difference between the end-diastolic and end-systolic volumes of the LV gives the stroke volume. Ejection fraction is defined as the stroke volume divided by the end-diastolic volume and expressed as a percentage.

Methods of assessment of EF by 2D echo:

Subjective Assessment: Since EF is a unitless ratio, it is often assessed by visual estimation, which in the hands of experienced echocardiographers has been found to have reasonable correlation with trackball measurements[17]. However, this does not measure actual LV volumes which are also important and is subject to error especially if there is irregular rhythm

or significant tachycardia.

LV Volume Measurement: Due to the complex shape of the LV, geometric assumptions have to be made in extrapolating volumes from 2D images. Various geometrical formulas have been used such as the area-length method, single-plane ellipsoid, biplane-ellipsoid and hemisphere cylinder[18], all of which have shortcomings and are based on the assumption that the ventricle will adhere to a predictable shape. Regional dysfunction further decreases the accuracy of these methods.

Simpson's Rule: With improvement of resolution in 2D echo, direct assessment of LV volumes in apical views has become possible and the most commonly used method now for estimating EF is the Simpson's rule. The endocardial border is defined in an apical 2 or 4 chamber view in end-diastole and end-systole. The ventricle is divided into a series of disks along the long axis from apex to base and the LV volume is obtained by summation of the volumes of individual disks[19]. This method is not completely free from geometric assumption as each disk is expected to be circular. Foreshortening of the LV apex will result in incorrect measurement of EF. Other potential pitfalls include failure to direct the ultrasound beam through the center of the LV resulting in a tangential cut and inaccurate tracing of the endocardial borders due to myocardial dropout or poor image quality which results in erroneous volumes. Tissue harmonic imaging[20] and contrast echocardiography[21] help to overcome the latter problem to some extent. Intravascular contrast agents significantly improve endocardial border detection and EF measured using contrast echo has been shown to correlate with 3D echo and MRI[22]. Also, techniques for automated identification and tracking of the endocardial border and automatic quantification of LV volume, such as acoustic quantification[23] and colour kinesis[24] have been developed but these require calibration and have not come into routine use.

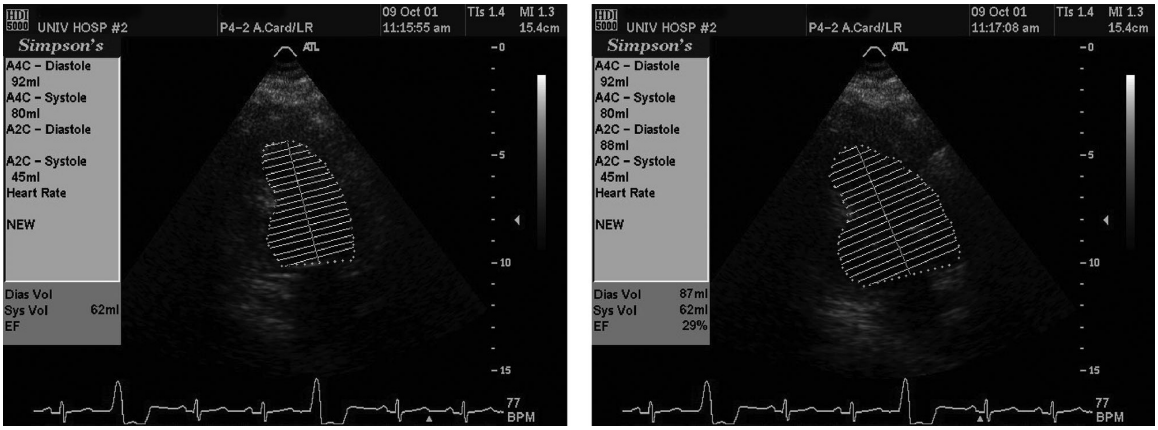


Figure1. Simpsons method: Systolic and diastolic frames

Advantages of EF:

Ejection fraction is widely used as it is easy to obtain and has been shown to robustly predict mortality,[3] i.e. lower the EF, lower the survival. EF has been shown to be more important than the number of diseased coronary arteries[25] or the degree of perfusion defects[26]. EF has not only prognostic implications, but also guides therapeutic decision making. Many large multicenter trials have used EF as the sole measure of LV function. It has become the gatekeeper for biventricular pacing, defibrillator implantation[6] and drug therapy initiation. Thus, a lot of weightage is given to this particular parameter.

Disadvantages:

Technical difficulties in measurement, especially endocardial border definition have already been mentioned. Interobserver variability exists in measured EF. In addition, EF is dependent on both preload and afterload. In aortic stenosis, the increase in afterload due to outflow obstruction falsely attenuates the EF, which improves after the obstruction is removed. In mitral regurgitation, the low afterload due to decompression of the LV into the dilated left atrium (LA) falsely augments EF[27]. After the mitral valve is repaired or replaced, the EF could deteriorate as the route into the low pressure LA sink is closed. Thus for the same degree of ventricular contractility, EF can differ depending on the loading conditions. This makes serial follow up studies difficult as loading conditions may not be the same and actual ventricular

volumes may be more useful to track remodelling[28]. In a situation of acute ischemia such as during an acute coronary syndrome, non ischemic segments may become hyperkinetic and compensate for the poorly contracting ischemic area, with overall EF remaining in the normal range. As the function of the ischemic segment recovers, hyperkinesis would resolve and those segments would revert back to their normal state of contraction. All this while, EF has not changed, even though considerable pathophysiological processes have occurred. Increasingly, use of EF alone has been considered insufficient as a comprehensive measure of LV systolic function especially in view of availability of new echocardiographic methods and better understanding of the dynamics of LV function in recent times[29].

Load corrected parameters:

As mentioned above, loading conditions affect measurement of the LV function and there have been attempts to derive parameters which correct for the loading state. LV midwall shortening expresses the stress shortening relation of the ventricle. The use of midwall shortening is less dependent on LV geometry than are endocardial measurements. The other approach is to draw pressure-volume loops to show the association between loading and inotropic state. The end systolic pressure volume relationship is drawn or LV wall stress against LV dimension can be plotted. An increase in the slope of the curve corresponds to increased contractility and decrease corresponds to reduction in contractility. These parameters are not easy to measure non-invasively and are not used in routine practice[18].

Three Dimensional Echocardiography:

The development of three dimensional echocardiography (3D echo) has marked a major step forward in accurate assessment of ventricular volumes and function, given that 2D echo has shortcomings in capturing the complex geometry of the LV. In 3D echo, cardiac structures are

shown in relationship to each other in all three spatial dimensions.

Earlier approaches to 3D echo used a series of 2D images to reconstruct a 3D data set using offline software. The quality of 3D reconstructions from 2D images depends on a number of factors, including the intrinsic quality of the ultrasound images, the number (or density) of the 2D images used to reconstruct the 3D image, the ability to limit motion artifact, and adequate ECG and respiratory gating. In general, the greater the number of images obtained (i.e., the smaller the space intervals between images), the better the 3D reconstruction. However, increasing the number of images also lengthens the acquisition time, which can potentially introduce motion artifact. Consequently, the optimal number of images necessary for 3D reconstruction depends on the cardiac structure being examined and the resolution required. For example, 4 to 6 serial images are usually adequate for volume reconstructions of the left ventricle (LV), whereas more images are often needed to visualize more complex, rapidly moving structures, such as mitral and aortic valves.

The development of Real Time 3D (RT3D) echocardiographic systems circumvents many of the disadvantages of reconstructive methods. RT3D echocardiography uses a transducer with ultrasound elements arranged in a grid fashion. Modern 3D transducers have matrix-array transducer technology with more than 3000 imaging elements which obtain a pyramidal volume data set and give images of good quality. Some form of gating needs to be used in obtaining volumetric data. There are three acquisition modes in RT3D- namely, real time (narrow), zoom (magnified), and wide angle. The real-time mode displays a pyramidal data set of approximately 50° × 30°. The zoom mode displays a smaller, magnified pyramidal data set of 30° × 30° at a higher resolution. The wide-angle mode provides a pyramidal data set of approximately 90° × 90°, which allows inclusion of a larger cardiac volume[30].

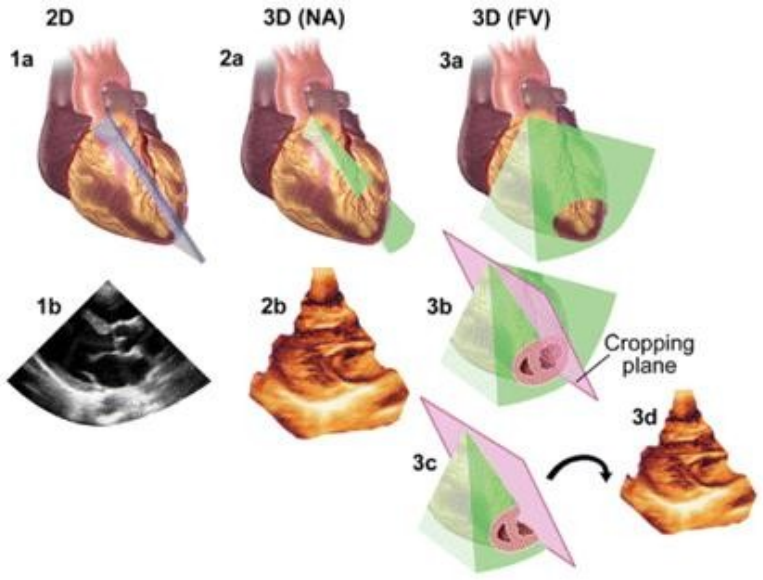


Figure 2. Progression from 2D imaging to 3D narrow-angle (NA) to 3D full-volume (FV) imaging.

Measurement of LV Volumes & function:

The wide-angle acquisition mode can be used to acquire the entire LV volume, from which a detailed analysis of global and regional wall motion can be done. Images may be displayed with either orthogonal long-axis views or multiple short-axis views. Intravenous contrast can be used as in 2D to better define the endocardial border. Multiple studies have validated the volumes measured by 3D against MRI and other modalities[31, 32]. It has been shown to be superior to 2D echo in measurement of ventricular volumes especially in abnormally shaped ventricles; however the challenge has been to improve the level of accuracy to the extent that

it impacts clinical decision-making over and above the information provided by 2D.

Right Ventricle: As the right ventricle has an asymmetrical pyramidal shape, assessment by 2D echo has limitations as it does not conform to geometric assumptions. Three dimensional imaging of the entire RV, especially with real time 3 D echo holds potential to more accurately assess RV function. Studies done using 3D echo involving offline processing of 2D data have demonstrated improved accuracy in assessing the RV[33].

The main limitation of 3D echo has been the difficult process of reconstruction using data from multiple 2D image sets, where even minor changes in transducer position will significantly affect image quality and endocardial definition. The availability now of faster processors and improved computer algorithms which allow real time 3D data acquisition has been more accurate. 3D echo is likely to be the future technology of choice to assess ventricular volumes and remodelling but the technology is not readily available at present.

Regional Function Assessment by 2D echo:

Subjective Assessment:

As echocardiography is frequently used to assess coronary artery disease, where perfusion is deficient to certain areas of the myocardium, assessment of regional function is particularly important. Subjective assessment can be done by describing regional wall motion abnormality (RWMA) i.e. the contractility of specific segments as normal, hypokinetic, akinetic or dyskinetic. The American Society of Echocardiography has proposed a standard 16 segment model for description of RWMA. Recently a 17th segment, namely the true apical segment has been proposed. The area affected gives an idea of the probable culprit coronary artery (fig 3). A semiquantitative method is the wall motion score index (WMSI) in which motion is scored

as 1 for normal, 2, 3 and 4 for hyokinesia, akinesia and dyskinesia respectively. The total score thus obtained is divided by the number of segments analyzed to obtain the WMSI. This acts as an index of global LV function and has been shown to correlate with prognosis[34].

Quantitative methods:

In order to introduce an element of objectivity, certain quantitative methods to assess regional function have been proposed.

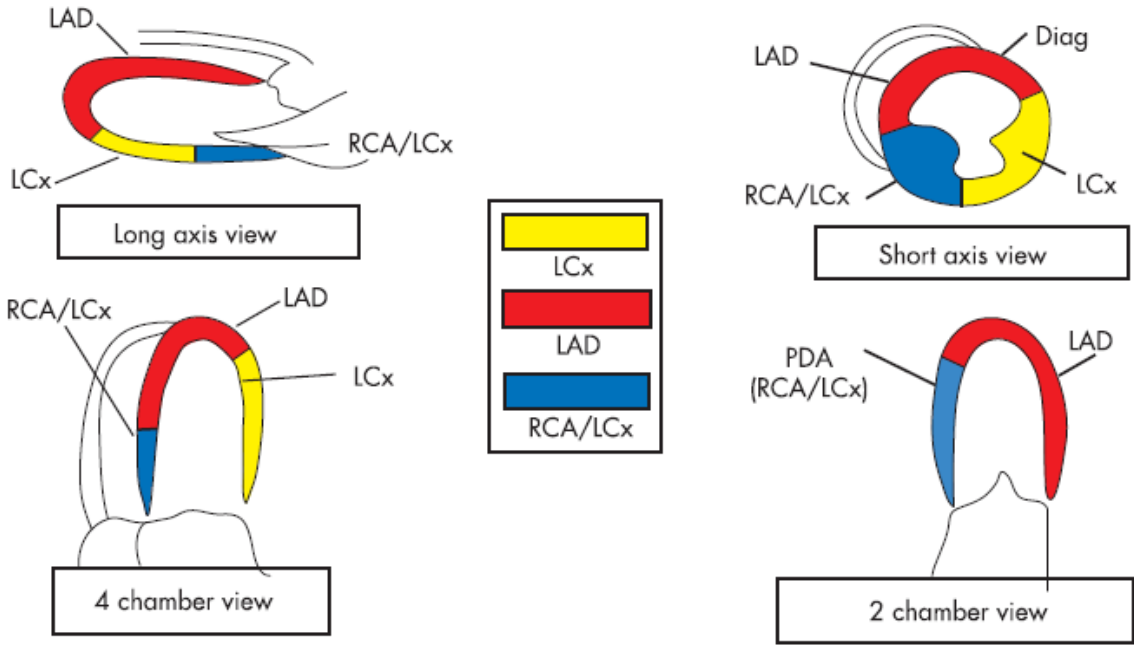


Figure.3 The 16 segment American Society of Echocardiography model for characterization of regional LV function, and usual coronary artery distribution of the segments.

1. Center line method- In this, the end diastolic and end systolic endocardial borders are traced and superimposed on each other. A center line is interpolated and the distance from this center line of different points in the endocardium in systole and diastole can be measured

by a series of chords extending perpendicular to the center line. This gives an idea of the displacement from

diastole to systole. This has also been called chordal shortening method. This method has shortcomings and is also time consuming.

2. Colour Kinesis method- This method uses acoustic quantification to define the border based on the difference in backscatter between the LV cavity and the endocardium. The excursion of the myocardium is tracked in successive frames and each is given a different colour code. The resultant display is overlaid on the 2D image and displacement calculated as segmental area shrinkage, is portrayed as stacked histograms. This method requires good image quality. Rotational and translational (movement of the heart within the chest cavity) movement of the heart contributes to errors[18].

RWMA can be present without ischemia in conditions such as bundle branch block, pacing, pre-excitation and post cardiac surgery. However, in these conditions, systolic thickening is preserved, which is almost invariably affected in true regional dysfunction.

DOPPLER EVALUATION OF LV FUNCTION:

Doppler measurement of flow can be used to assess LV function. The simplest technique is to calculate stroke volume by measuring the time velocity integral (TVI) of the LV outflow tract (LVOT), which is then multiplied by the cross sectional area of the LVOT to obtain volume. Comparison of left and right sided ejections by this method can be used to calculate their ratio (Qp/Qs) in congenital heart disease. Though it is simple, small errors in measuring the dimension of the LVOT would result in large variations in the final volume measured. Another useful method is the rate of rise of pressure (dp/dt) in the LV. The longer it takes to develop pressure, the worse the contractility (slower slope correlates with worse function). Peak LV positive dp/dt occurs typically in early systole before the aortic valve opens, thus

limiting the influence of afterload. Mitral regurgitation needs to be present in order for dp/dt to be measured by echo. It is determined by measuring the time it takes for the mitral regurgitation jet velocity to increase from 1 m/sec to 3 m/sec which represents the time taken for a pressure change of 32 mm Hg to occur. The dp/dt is then calculated as 32 divided by the measured time. The negative dp/dt measured over the second half of the curve is an indicator of diastolic function and relaxing properties of the ventricle. Dp/dt overcomes the problem associated with using EF in a patient with significant MR which was described earlier. It has been found to be an independent prognostic indicator in heart failure[35] and can help predict the occurrence of LV dysfunction after mitral valve replacement[36].

The myocardial performance index (MPI or *Tei* index) is a relatively load-independent measure of LV function[37]. It is calculated as the sum of the isovolumic contraction time (ICT) and isovolumic relaxation time (IRT), divided by the ejection time (ET). It is measured using the Doppler inflow of the mitral valve and that of the LVOT as shown in figure 4. This is said to be a measure of both systolic and diastolic function[38] and is useful in assessing right ventricular performance also[39].

Using the Doppler profile of mitral valve inflow, parameters of diastolic function can also be calculated such as the early filling (E) and atrial (A) wave velocities and the deceleration time of the LV. The pulmonary and hepatic vein flow profiles are also useful in measuring diastolic function.

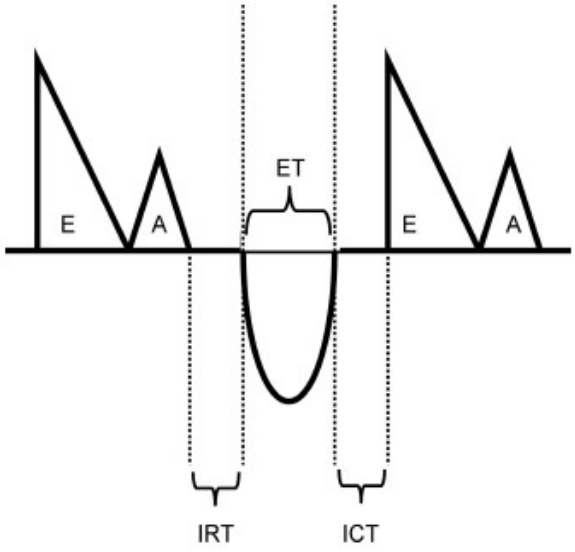


Figure 4. Tei Index measurement

Measurement of wall stress:

Wall stress is defined as the force over each unit of cross sectional area and the force is determined by pressure in the ventricular cavity. As it accounts for both wall thickness and pressure generation, it is relatively afterload-independent and has been used for measurement of myocardial contractility. It can be calculated globally or regionally, as well as in mutually orthogonal planes i.e. meridional stress imposed by long axis (base-apex) shortening and circumferential stress in the minor axis[40, 41]. Measures of wall stress are most useful in ventricular pressure or volume overload states such as hypertension, aortic stenosis and mitral or aortic regurgitation.

TISSUE DOPPLER IMAGING:

Tissue Doppler imaging (TDI) is an exciting new tool that is easy to perform and reproducible[42]. This technique uses specific receiver gains and frequency filters to eliminate blood motion and track the actual motion of the myocardial wall. Myocardial tissue velocity is

typically an order of magnitude below that of blood velocity. The signal from tissue movement is displayed as a colour display overlaid on the anatomical image itself, or more commonly pulsed Doppler is used for spectral analysis of TDI velocities which is more reliable. TDI has good spatial and temporal resolution. A number of parameters can be derived from TDI in systole and diastole which have been proposed to be useful in a variety of cardiac diseases[43]. Magnitude of excursion of the mitral annulus has been shown to be a sensitive measure of LV function; is affected early by ischemia[44] and correlates with LVEF[45]. Measuring this using M-mode is tedious. Peak systolic velocity in ejection period measured using TDI at the mitral annulus (Sa) or at myocardial segments (Sm) is easier to perform. Peak myocardial systolic velocity averaged from 6 sites around the mitral annulus correlates well with LVEF, and a cut-off of >7.5 cm/s had a sensitivity of 79% and a specificity of 88% in predicting normal global LV function[46]. Reduced TDI velocities have been shown to be useful in detecting mild impairment of LV systolic function in those with a normal EF or so called diastolic heart failure[47] and in diabetic subjects without overt heart disease[48] . Reduced TDI velocities can be seen in subjects with hypertrophic cardiomyopathy mutations even at the time of subclinical disease when

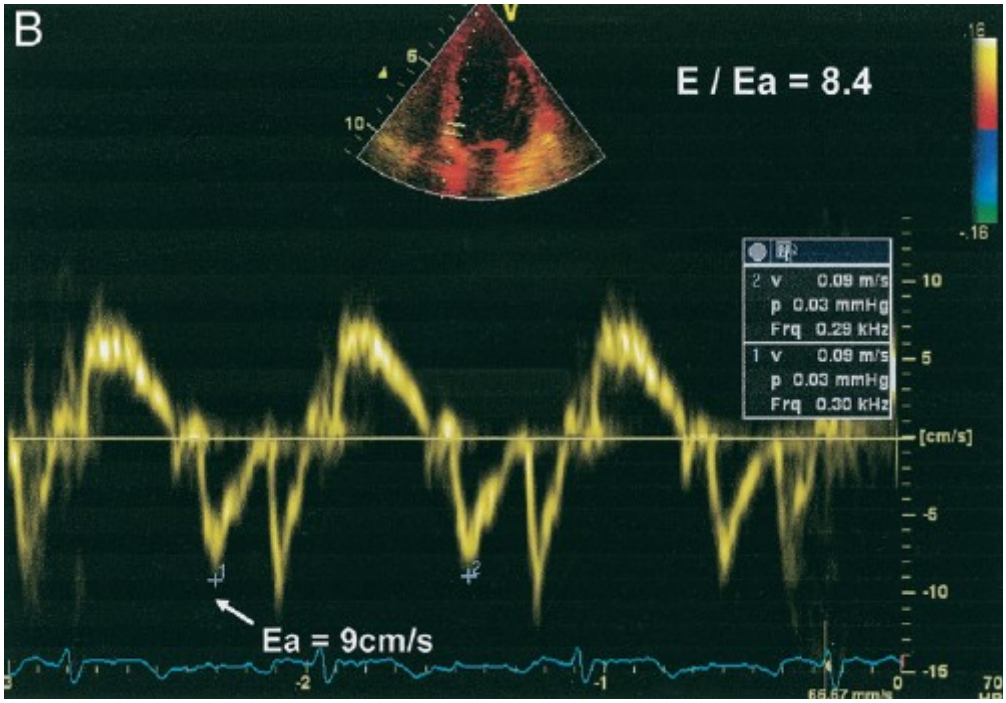


Figure 5. TDI of septal mitral annulus

hypertrophy is not present[49]. Hence TDI can be used for early identification of hypertrophic cardiomyopathy.

Peak early (Ea) and late (Aa) mitral annular diastolic velocities can also be measured as indices of diastolic function. Ea is a marker of the speed of myocardial relaxation[50]. Reduction in Ea is one of the earliest indicators of diastolic dysfunction and it remains reduced at all stages of diastolic dysfunction[51, 52]. Thus Ea remains low even when there is pseudonormalization or a restrictive filling pattern by conventional mitral inflow Doppler. Hence the E/Ea ratio increases as diastolic dysfunction worsens and has been shown to correlate with LV filling pressure or pulmonary capillary wedge pressure (PCWP) [53]. E/Ea ratio greater than 15 is said to correlate with a PCWP of > 20 mm Hg. This ratio predicts survival after acute myocardial infarction[54] and has incremental prognostic value over EF[55]. Reduced Ea has been shown to be associated with adverse outcome including mortality and hospitalization independent of clinical risk factors and Doppler derived indices such as

deceleration time in patients with heart failure and also in those with hypertrophy and normal ejection fraction.

Reduced annular systolic and diastolic velocities are independent predictors of mortality, with Ea being a stronger predictor. Reduced velocities of < 3 cm/sec were found to be associated with a lower survival[56]. They also add incremental risk above wall motion scores in coronary artery disease and predict cardiac mortality. In patients with mitral regurgitation, reduced lateral mitral annulus systolic velocity could predict those who would develop reduction in EF after mitral valve replacement surgery.

TDI has been used to measure peak myocardial displacement and velocity in those undergoing dobutamine stress echo. Reduced tissue velocity of < 6 cm/sec in stress echo has been shown to correlate with mortality and risk of acute coronary events even when assessment by wall motion score did not show a significant difference[57]. Another important application of TDI is in measuring mechanical dyssynchrony in heart failure subjects. The time to onset or peak of systolic velocity is assessed in different segments and the delay calculated[58, 59]. Dyssynchrony measured by TDI predicts clinical outcomes in heart failure even in subjects with narrow QRS[60] on ECG and can help predict response after CRT[61].

The main limitation of tissue Doppler is the angle dependency of the technique, as accuracy depends on good alignment of the pulsed Doppler in line with the region of interest. Assessment of apical function is therefore unsatisfactory. Also, use of tissue velocity examines tissue movement with respect to the transducer and not with respect to adjacent tissue. The movement of a given segment is influenced by the motion of the adjacent segments which is called the “tethering effect”. Thus, an ischemic poorly functioning segment could be “pulled along” because the adjacent segment is hyperkinetic. Strain and strain rate imaging help to overcome this limitation.

STRAIN AND STRAIN RATE:

Strain or myocardial deformation imaging is conceptually appealing as it does not rely on motion with respect to the transducer but the relative motion between two segments within the myocardium. Two tissue Doppler samples can be recorded within the LV wall; if the sample volumes are moving apart, tension is produced just as if a rubber band is being stretched (positive strain). If the points are moving towards each other, then it would be as if the rubber band is being collapsed and tension decreases (negative strain). Thus, positive strain corresponds to relaxation and negative strain corresponds to contraction. Raw Doppler information provides the rate of change of length of tissue (distance over time) or strain rate. A two dimensional assessment looking strictly at only length gives strain.

Strain & strain rate can be measured by TDI[62] and more recently speckle tracking (described later). Strain Rate (SR) is a more sensitive measure than strain because a weaker contraction could theoretically reach the same peak strain, but at a slower rate. However, SR is noisier, limiting its ability to differentiate normal from abnormal. Determination of timing intervals and peak values in both longitudinal and radial views for both strain and SR can be obtained and compared with established normal values[63, 64]. Measurements of myocardial deformation with these techniques have been validated using microcrystals and magnetic resonance[65, 66].

Strain and strain rate can be potentially used to identify viable myocardium[67] and early ischemia[68]. Reduction of strain and SR has been correlated with myocardial fibrosis which itself is a marker of adverse cardiac risk[69]. It may also be useful as an indicator of subclinical disease[70] and in assessing response to therapy[71]. Though implications of strain responses to therapy are not well established, it seems likely that an improvement in deformation is likely to have a beneficial outcome.

Disadvantages of strain & SR are the low signal to noise ratio and angle dependence.

Significant data storage and computational ability is required for strain & SR studies. SR seems to be relatively independent of heart rate (chronotropy) [72] and relatively afterload-independent[70], but it would likely be preload-dependent, as initial diastolic dimension would be expected to affect strain by the Frank-starling principle. Improvement in techniques and further studies would likely delineate the full potential of strain rate imaging.

SPECKLE TRACKING ECHOCARDIOGRAPHY:

Speckle tracking echocardiography (STE) has recently been introduced as a novel method for quantification of myocardial performance. It is angle-independent in contrast to TDI[7].

Speckles are natural acoustic markers that occur as small and bright elements in conventional grayscale ultrasound images[73]. They are produced as a result of constructive and destructive interference of ultrasound, back-scattered from structures smaller than a wavelength of ultrasound[74]. These speckles are distributed equally around in the myocardium on the ultrasound image and can be identified and followed in consecutive frames during the heart cycles. Software that has the ability to assess myocardial strain, strain rate, velocities and displacement from these speckles has recently been developed[75]. Different speckle tracking algorithms have been validated in experimental and human studies[76, 77].

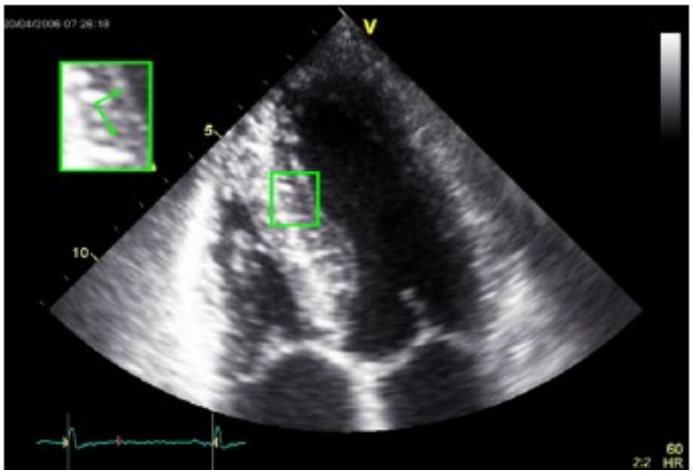


Figure 6. Myocardium from a 4 chamber view enlarged to show speckles

Longitudinal and radial strain can be estimated accurately by STE; in addition, myocardial velocities and displacement of the mitral annulus can be measured. Circumferential strain can also be measured due to angle-independency of the method. STE has also been used to predict response to cardiac resynchronization therapy and a recent clinical study demonstrated that assessment of radial strain by STE may quantify dyssynchrony and predict immediate and long-term response to cardiac resynchronization therapy[78]. A limitation of STE is that the time resolution in studies using STE has been in the range of 60-100 frames per second to optimize speckle quality. However, higher frame rates may be needed to reliably measure myocardial strain and velocity.

STE technology is still evolving and few systematic studies are available, but so far it seems to provide an accurate, simple and direct measure of myocardial deformation and velocity. Thus it has the potential to become a bedside clinical tool. Another novel technology that further builds upon STE is velocity vector imaging (VVI) which is described below.

VELOCITY VECTOR IMAGING:

Velocity Vector Imaging (VVI) is a visual and quantitative method for assessing the dynamics of cardiac motion which uses the information within the image to determine tissue motion throughout the cardiac cycle.

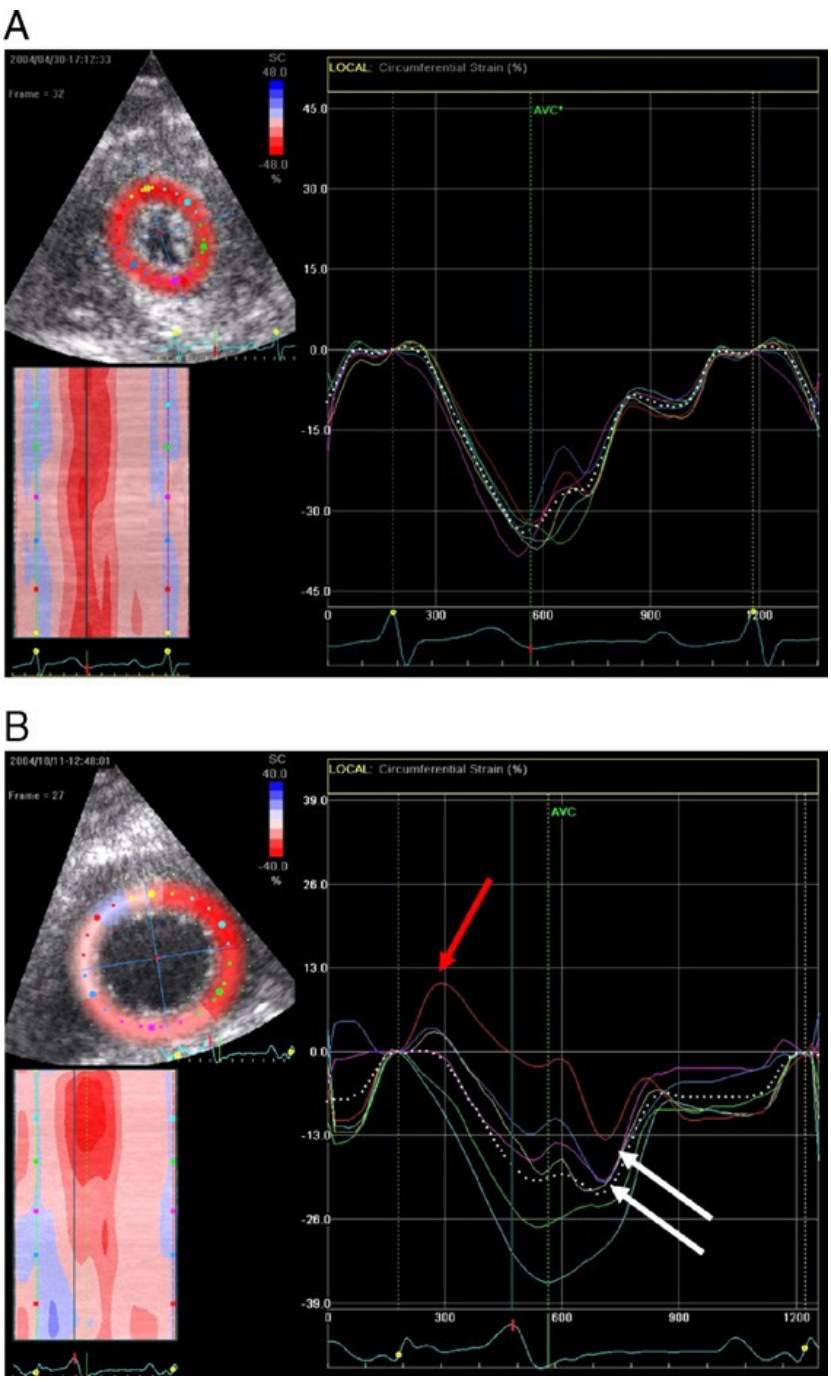


Figure 7. Circumferential strain by STE. A, Circumferential strain from the apical LV level in a healthy individual. Note the homogenous circumferential distribution of normal systolic strain. B, Circumferential strain at the LV apical level in a patient with a LAD-related myocardial infarction. Note reduced systolic shortening (strain) in the anterior, septal, and inferior segments, with marked postsystolic contraction (white arrows). In addition, in the septal segments, there is early systolic stretching indicating dyskinesia (red arrow).

Technology:

VVI is not a simple speckle tracking algorithm alone, but also includes global motion coherence, consistency of periodicity between cardiac cycles and other techniques. VVI extracts cardiac motion by tracking a user-defined trace which is typically drawn along an endocardial border. The trace is tracked throughout one or more cardiac cycles by successive applications of a series of tracking steps. By tracking key reference points, inward and outward border motion, motion of tissue along the direction of the border, and by constraining the tracking to be periodic over the R-R interval, VVI computes robust estimates of the cardiac motion. At each stage of the tracking, Fourier analysis is used and applies the constraint that the trace must return to the same location at the subsequent cardiac cycle[79]. Thus, the borders are not “detected”, but “tracked” over time. Prerequisites to use the VVI algorithm include a good quality 2D image encompassing the entire region of interest and at least one full R-R interval must be captured to enable the algorithm to use the periodicity of the cardiac cycle.

Image Display:

Yellow velocity vectors, placed on the B-mode image, indicate the direction and relative speed of the tissue, with longer arrows indicating proportionally higher velocities (fig 8). These velocity vectors are updated every frame to show velocities of the tissue region throughout the cardiac cycle. In addition, a graph of velocity vs. time is displayed showing the directional velocity relative to a user moveable reference point. For example, when the reference point is placed in the center of the left ventricular chamber, as in a short axis view, the radial velocity is seen.

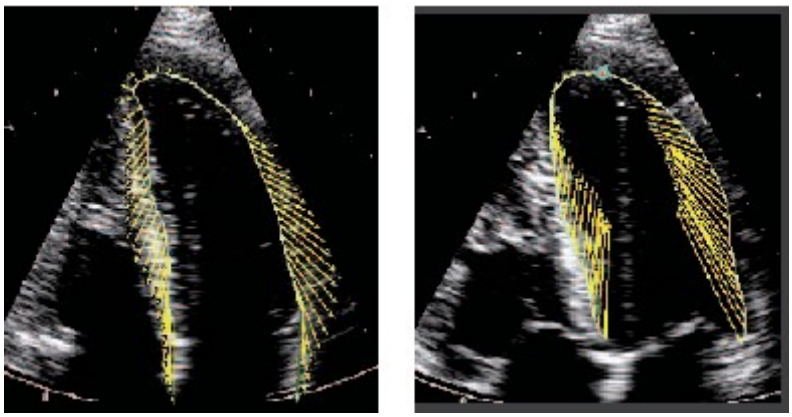


Figure 8. VVI analysis of a normal heart in diastole and systole

Strain and strain rate are calculated along the border. Strain is computed from the changing distance between the tracked trace points plus the differences in velocity of the tissue moving behind these points. Thus, strain reflects the relative change in distance between points of tissue along the border, reflecting lengthening or shortening.

VVI can also be used to assess cardiac dyssynchrony. VVI displays the tangential and radial velocity, strain, strain rate, and tangential and radial displacement for different myocardial segments. The time to peak value of these measurements can be obtained and displayed; thus lack of synchrony in motion of the different segments can be identified. This can also be easily visually appreciated by observing a trace overlaid with velocity vectors showing the speed and direction of movement of different regions (figure 9).

It has been proposed that VVI would have additive value over TDI in analysis of dyssynchrony especially with regard to circumferential and radial mechanics of the ventricle and also be useful to assess resynchronization after CRT[8]. Cannesson et al. found that opposing wall peak velocity delay of ≥75 milliseconds predicted response after CRT with a sensitivity of 85% and specificity of 80%[80].

By reliably tracking the endocardial border, VVI can compute ventricular volumes and ejection fraction using Simpsons rule. Regional function can be assessed by dividing each side of the trace into 3 segments of equal length and identifying regions with abnormal contractile function (figure 10). Another potential application of VVI is in assessing rotational movement of the LV. Along with movements along the longitudinal and radial axis, during every contraction, the LV apex rotates in a counterclockwise direction, while the base rotates in a clockwise direction. The term *LV torsion* has been applied to this movement, which is technically difficult to measure using conventional echocardiography.

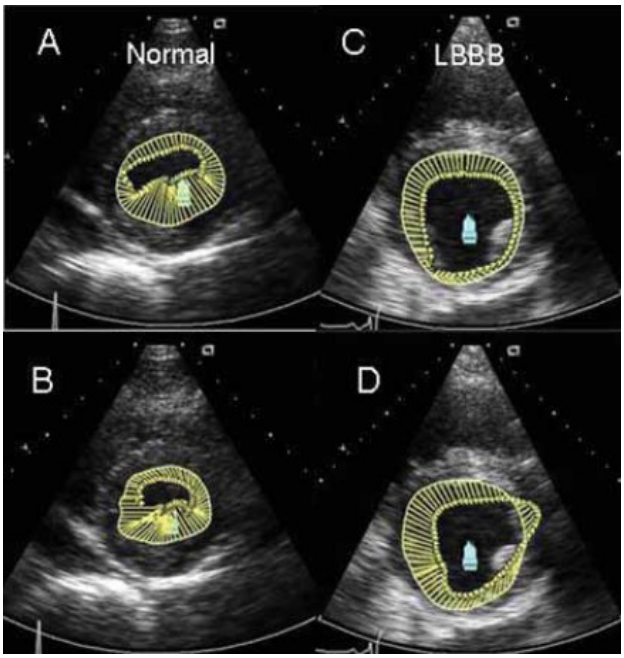


Figure 9. Radial velocity vectors in the apical short axis view from a normal (left panel) and a patient with LBBB (right panel). In the normal patient, in early/mid systole (A) and in late/end systole (B) the radial vectors are of similar magnitude and direction. In LBBB, in early/mid systole (C) the septal vectors are of higher magnitude than lateral radial velocities, in late systole (D) the septal vectors have peaked whereas the lateral wall vectors are directed in the opposite direction (dyssynchronous).

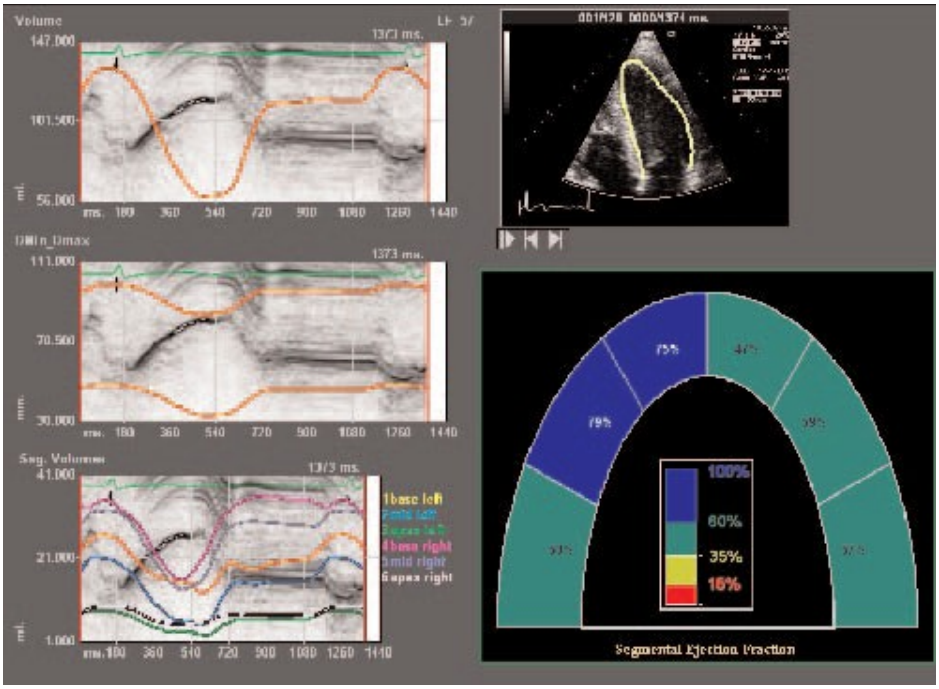


Figure 10. Global and regional EF by VVI

Using velocity vector display in short axis views at the apex and base, rotational movement can be visualized and quantified. Measurement of LV torsion is an area of active research using speckle tracking echocardiography[81, 75] and VVI is likely to contribute to this in future. Other potential areas for use of VVI include assessment of right ventricular function[82], left atrial mechanics, stress echocardiography and fetal echo[79].

Other Methods to assess LV Function:

Though echocardiography is the most widely used, other modalities are available to measure LV function. A brief mention is made of these.

Cardiovascular magnetic resonance (CMR)

This is a noninvasive 3-dimensional imaging technique which can provide morphologic and functional information as well as tissue characterization without the use of ionizing radiation or nephrotoxic contrast agents. It has a high accuracy and reproducibility and is optimally suited

to quantify structural and functional abnormalities and to follow a patient over time. A specific advantage of CMR over echo is the ability to acquire images in any selected plane along the specific cardiac axes or any other, which makes it possible to thoroughly study cardiac morphology and function irrespective of patient build or habitus.

Assessment of LV function: Bright blood gradient echo sequences, obtained during a 15- to 20-second breath-hold, are used to cover the entire LV with short-axis views from the mitral plane and slice thickness not exceeding 10 mm. Regional myocardial function is best assessed using a unique MR technique called myocardial tagging. Special modulation of magnetization is obtained by applying a radiofrequency pre-pulse that labels the heart muscle with a dark grid and enables three-dimensional analysis of cardiac rotation, strain (in the subendocardial, midwall, and subepicardial layers), displacement, and deformation of different myocardial layers during the cardiac cycle . The tags can be applied immediately after the R-wave on the electrocardiogram to image systolic function or in late systole to image diastolic function[83].

Viability: Contrast-enhanced MRI is rapidly evolving as a means of accurately predicting myocardial viability. On first-pass perfusion images, an area of hypoenhancement within the infarcted region, correlating with microvascular obstruction is observed. A second enhancement pattern is noticed at 10 to 30 min after contrast injection (delayed hyperenhancement [DHE]). The DHE can be used to detect changes after acute and chronic myocardial infarction. An association between transmural extent of DHE detected by magnetic resonance and functional recovery after revascularization has been shown. End diastolic wall thickness and systolic thickening can also be used as markers of viability[84]. This can be evaluated using dobutamine stress MRI.

Further, imaging of the coronary arteries by MRI has been developed and though currently it

is not ideal, it shows future promise in becoming a non-invasive modality to view the coronary tree[85].

Thus, CMR has been shown to have good accuracy in measuring LV volumes as well as in assessment of viability, but is constrained by availability of equipment and cost[86].

Computed Tomography **(CT)**:

Conventional CT lacks the spatial or temporal resolution for adequate imaging of the heart; however recent use of multidetector array CT (MDCT) scanners and ECG gating has improved the imaging capability of CT.

Wall motion abnormalities and areas of hypoperfusion can be assessed on the short-axis, four-chamber or two-chamber views, along with evaluation of the volumes and ejection fraction. This is done by performing a multi-phasic reconstruction at 5% intervals from the base to the apex of the heart, at 8mm intervals with 8mm thick slices. This yields 10 to 12 "sections", each of which contains images at 5% intervals to allow smooth cine viewing. Overcoming cardiac motion artifacts is a significant problem and often heart rate needs to be lowered by the use of beta blockers to achieve adequate resolution in imaging[87]. Studies have shown fair correlation between LV volumes and function obtained by MDCT and MRI[88] as well as conventional echo and nuclear gated SPECT[89]. Further, with the use of 64 slice CT, high resolution non invasive imaging of the coronary arteries has become possible and

has already entered the clinical arena. It has been shown to have good sensitivity and specificity compared with conventional angiography for detection of significant coronary artery disease[90]. Its real advantage lies in a consistently high negative predictive value observed in

most studies, which allows one to exclude coronary artery disease with a high degree of confidence in the presence of a normal CT angiogram.

However, at present there is not much data regarding the ability of CT derived LV function to predict risk in clinical practice[18]. Also the imaging is hampered by the presence of high heart rate, arrhythmia and extensive calcification. Radiation exposure from MDCT has also been an issue of concern and the technique requires use of iodinated contrast. Nevertheless, combined assessment of coronary anatomy and LV function by MDCT is likely to become useful in the diagnostic armamentarium in evaluating coronary artery disease.

***Nuclear Imaging**:*

Nuclear imaging techniques to measure ventricular function include first pass ventriculography, equilibrium radionuclide ventriculogram (gated blood pool scanning), and gated single photon emission computed tomography (SPECT), during myocardial perfusion scanning with thallium-201 or Tc99m-sestamibi. These methods have been shown to have prognostic value after a myocardial infarction[91] and add to risk stratification[92]

SPECT is a highly sensitive and moderately specific tool to detect coronary artery disease. Wall motion and systolic thickening can also be seen to assess regional myocardial status. LV volumes and EF measured by gated SPECT has been shown to correlate well with other techniques. EF can be calculated both at rest and post stress and the latter has incremental prognostic value over data provided by the perfusion study. Gated SPECT can detect wall motion and systolic thickening changes induced by inotropic stimulation; thus it can assess contractile reserve and myocardial viability.

In recent times, gated SPECT is being used more and more to measure LV function alone in non coronary artery disease settings like dilated cardiomyopathy and has been used to predict response to therapy. Potential disadvantages with SPECT include presence of tissue

attenuation artifacts and radiation exposure. Extensive perfusion defects could reduce the accuracy of LV volume and EF measurement. This has been a rapidly growing field with new breakthroughs in technology and could possibly become a “one- stop-shop” for assessing coronary artery disease by combining CAD detection, LV function assessment and viability[93].

Relevance of the present study

From the preceding discussion, it is clear that a variety of methods are available to measure LV systolic function. Left ventricular geometry is complex and contraction in systole involves movement in more than one axis. The arrangement of myocardial fibers is not uniform across the wall of the LV; subendocardial and subepicardial muscle bundles are aligned longitudinally, with a slight spiral arrangement, and midwall fibers are aligned circumferentially. The latter group of fibers are responsible mainly for short axis or radial contraction of the left ventricle, whereas the former cause long-axis contraction (figure 11)[29]. In addition, twisting and untwisting of the LV (torsion) also contributes to global LV function. Hence, assessment of this complex movement requires judicious application of different echocardiographic modalities and conventional 2D echo alone is no longer adequate in this regard. The development of tissue Doppler imaging, strain, strain rate and speckle tracking echocardiography represent important developments in understanding and measuring LV mechanics.

Figure 11. Normal LV myocardium showing longitudinal fibers running between the apex and the mitral ring and occupying the subendocardial and subepicardial layers

As a simple to understand, easy to measure and powerful prognostic number, the ejection fraction is still one of the key measures of LV function in spite of its limitations. However, technical difficulties in measurement especially with regard to proper endocardial border definition can hamper accuracy. It is therefore important to evaluate new technologies which may have a potential role in this regard. VVI is an exciting new application of speckle tracking echocardiography that is able to measure velocity and direction of tissue motion using a complex tracking algorithm. VVI can efficiently track the endocardial border and has been said to have clinical utility in measuring LV volumes, EF and regional function. However, there are no studies which have systematically evaluated the accuracy of EF measured by VVI.

Hence this study was performed comparing ejection fraction measured by VVI to standard 2D echo and nuclear gated SPECT in a cohort of patients. This study is likely to give insights into the issues with the practical use of VVI in a clinical setting and the need for improvements if any.

METHODOLOGY

The study was performed among outpatients from the cardiology department of Christian Medical College, Vellore; a tertiary care institute in South India. Subjects who presented to the outpatient area for evaluation of suspected coronary artery disease were prospectively recruited.

Inclusion Criteria:

Patients presenting to the outpatient department of Cardiology for evaluation of chest pain were eligible to be included in the study.

Exclusion Criteria:

1. Inability to obtain a good quality echo image due to a poor window or other factors.
2. Unwillingness to participate in the study.

Baseline clinical data including risk factors, history of previous myocardial infarction, previous coronary angiography and current drug list was collected in all patients. Patients underwent a 12 lead electrocardiogram and chest X-ray.

Echocardiography:

Conventional 2D echocardiography in long axis, short axis and apical views were performed, and the ejection fraction calculated using Simpson's rule. Patients were categorized as normal or having mild, moderate or severe LV dysfunction based on American Society of Echocardiography classification[94]. (Normal ≥55%, mild LV Dysfunction 45-54%, moderate LV Dysfunction 30-44%, severe LVDysfunction < 30%). Regional wall motion abnormalities were subjectively assessed and regions of reduced contractility described as hypokinetic, akinetic or dyskinetic.

VVI Analysis:

VVI analysis was performed using the Siemens Sequoia 512 machine (Siemens Medical Solutions USA, Inc.). After recording a 2D image of good quality, the LV endocardium was

traced manually in the apical 4 chamber view to provide the basic trace which the VVI algorithm then used to automatically track endocardial border movement. LV volume was calculated based on the volume of sixty-four disks whose diameters fit between opposing sides of the trace and are parallel to the plane defined by the trace endpoints (mitral plane). Regional volumes were computed by dividing each side of the trace into three segments of equal length and then dividing the disks into two portions using a line from the apex to the center of the base. This helps to identify regions with abnormal contractile function (refer Fig 9. of literature review).

Nuclear Imaging:

Each patient also underwent nuclear perfusion study by gated SPECT using technetium 99m-sestamibi from which presence and extent of regional ischemia was analyzed and ejection fraction was also calculated. In addition SPECT EF was calculated by another observer independently in 12 randomly selected patients to assess inter-observer variability.

Statistics:

Pearson's correlation coefficient was used to analyze the correlation between ejection fraction calculated by VVI, SPECT and 2D echo. The numerical relationship between VVI EF and SPECT EF was calculated using regression equation to get an idea of the magnitude of difference in measurements by the two modalities. Paired t test was used to analyze continuous variables and chi square test or Fisher's exact test to assess categorical variables. Significance was considered at a p value of ≤ 0.05. Statistical analysis was performed using SPSS version 10.

RESULTS

A total of 49 patients were studied. Table 1 shows the demographic characteristics of the patients studied.

The mean age of the subjects was 55.04 ± 8.78 years; they were predominantly male (87.8%). A little over 40% were diabetics and hypertensives and 40.8 % had suffered a previous ST elevation myocardial infarction (STEMI). Twenty of the subjects had undergone a coronary angiogram out of which 2 (4.1%) were normal, 4 (8.2%) had minor coronary artery disease; 2 (4.1%), 6 (12.2%) and 5 (10.2%) subjects each had single, double and triple vessel coronary artery disease respectively. SPECT showed evidence of ischemia in about 27% of patients and fixed (irreversible) defects in about 30% of patients.

Measurement of Ejection Fraction:

The mean ejection fraction (EF) calculated by VVI was 35 ± 12.08%, as compared to 54.2 ± 19.51% with SPECT and 50.3 ± 8.92% with 2D echo. The difference between the EF measured by different modalities was analyzed using the paired samples t-test. Table 2 shows the paired samples statistics comparing VVI EF with SPECT and 2D echo. As seen from the table, the mean EF measured by VVI was significantly less than that measured by the other modalities ($p<0.001$).

Table 1 Demographic Characteristics (numbers in brackets indicate percentages)

Age (mean± SD)	55.04± 8.78
Male	43 (87.8)
Diabetes	21 (42.9)
Hypertension	20 (40.8)
Smoker	15 (30.6)
Dyslipidemia	30 (61.2)
Angina	25 (51)

Dyspnea	22 (44.9)
NYHA Class I Class II Class III	13 (26.5) 33 (67.3) 3 (6.3)
Previous STEMI	20 (40.8)
Previous ACS (other than STEMI)	14 (28.6)
Q waves on ECG	15 (30.6)
RWMA by ECHO	17 (34.7)
Ischemia on SPECT	13 (26.5)
Aspirin	32 (65.3)
Beta blocker	28 (57.1)
Statin	35 (71.4)
ACEI/ARB	25 (51.1)
Nitrate	22 (44.9)

ACS = Acute coronary syndrome, ACEI = Angiotensin converting enzyme inhibitor, ARB = Angiotensin receptor blocker.

Table 2. Paired T-Test

Comparison Pair	Paired differences					t	df	Sig. (2 tailed)
	Mean	Std. Devn.	Std. error mean	95% confidence inerval of the difference				
				Lower	Upper			
SPECT EF- VVI EF	19.22	15.96	2.28	14.64	23.81	8.432	48	<0.001
2D EF- VVI EF	16.26	10.05	1.53	13.16	19.35	10.612	42	<0.001

The Pearson's correlation coefficient was used to look for a linear relationship between EF measured by VVI and the other modalities. Table 3 shows the statistics for Pearson's correlation coefficient for SPECT and 2D EF in comparison to VVI. There was a positive linear correlation between the VVI EF and SPECT EF (correlation coefficient 0.577; p=0.01) as well as 2D EF (correlation coefficient 0.573; p=0.01). Figure 1 shows a scatter plot that depicts this linear association between VVI and SPECT EF.

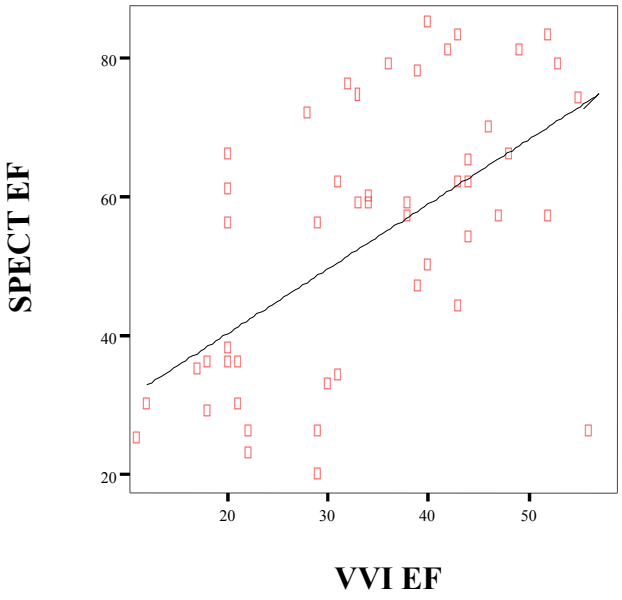
Table 3. Pearson's Correlation Coefficient Statistics

Modality	Mean	Standard Deviation	Pearson's correlation with VVI EF	Significance (2 tailed)
SPECT	54.22	19.51	0.577	0.01
2D	50.37	8.92	0.573	0.01
VVI	35.00	12.08	1.000	-

Assessment of LV Dysfunction:

Table 4 shows the relative proportion of patients with normal LV function, mild, moderate, or severe LV dysfunction as per the different modalities of measurement using American Society of Echocardiography criteria. For purposes of comparison, normal and mild LV dysfunction was clubbed as one group and moderate and severe LV dysfunction as another group. This is

Fig.1 Scatter plot showing the relation between VVI EF and SPECT EF



clinically relevant as therapeutic decisions would likely be quite different in these 2 categories. The Fisher's exact test was then used to look for a significant difference in the proportion of patients in each group; comparing VVI with SPECT and then VVI with 2D echo (Tables 5 &

6). There were significantly greater proportion of patients categorized as having moderate or severe LV dysfunction by VVI (75.5%) when compared to SPECT (34.7%; p= 0.026 vs. VVI) as well as 2D echo (32.7%; p=.0.037 vs. VVI). Figure 2 gives a graphic comparison of the proportion of patients with LV dysfunction using SPECT or VVI. As easily seen from the graphs, significantly more patients are clustered in the moderate and severe LV dysfunction groups by VVI.

Table 4. LV Dysfunction by 2D echo, SPECT and VVI (percentages in parentheses)

LV Function	2D echo	SPECT	VVI
Normal	27 (55.1)	28 (57.1)	2 (4.1)
Mild dysfunction	6 (12.2)	4 (8.2)	10 (20.4)
Moderate dysfunction	16 (32.7)	10 (20.4)	22 (44.9)
Severe Dysfunction	0 (0)	7 (14.3)	15 (30.6)

Table 5. Statistical Comparison of categorized LV function: SPECT & VVI EF

			2 categories VVI LV Dysfunction		
			none or mild	moderate or severe	Total
2 categories SPECT LV Dysfunction	none or mild	Count	11	21	32
		Expected Count	7.8	24.2	32.0
	moderate or severe	Count	1	16	17
		Expected Count	4.2	12.8	17.0
Total		Count	12	37	49
		Expected Count	12.0	37.0	49.0

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	4.874	1	.027	
Continuity Correction	3.455	1	.063	
Likelihood Ratio	5.763	1	.016	
Fisher's Exact Test				.026
Linear-by-Linear Association	4.774	1	.029	

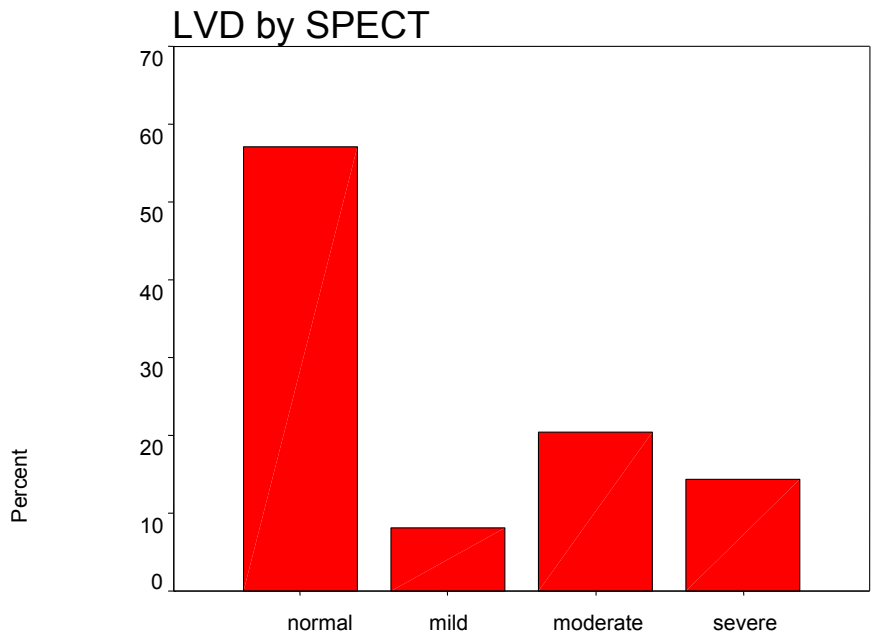
Table 6. Statistical Comparison of categorized LV function: 2D & VVI EF

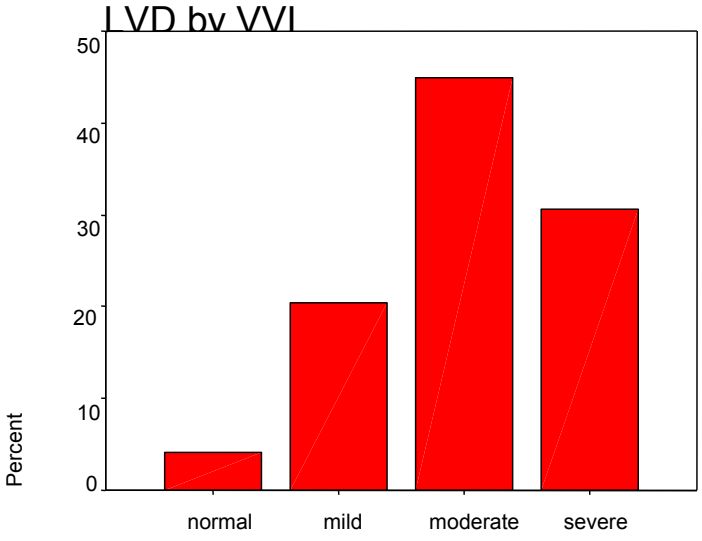
			2 categories VVI LV Dysfunction		
			none or mild	moderate or severe	Total
2D LV Dysfunction 2 categories	none or mild	Count	11	22	33
		Expected Count	8.1	24.9	33.0
	moderate or severe	Count	1	15	16
		Expected Count	3.9	12.1	16.0
Total		Count	12	37	49
		Expected Count	12.0	37.0	49.0

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)
Pearson Chi-Square	4.274	1	.039	
Continuity Correction	2.935	1	.087	
Likelihood Ratio	5.061	1	.024	
Fisher's Exact Test				.037
Linear-by-Linear Association	4.187	1	.041	
N of Valid Cases	49			

Figure 2. LV Dysfunction (LVD) by SPECT and VVI





Analysis of Regional Function:

While regional wall motion abnormality (RWMA) was assessed subjectively by 2D echo, regional EF was calculated using VVI as described earlier by dividing the trace into 3

segments of equal length on each side. These segments labeled 1 to 6 correspond to basal inferoseptum, mid inferoseptum, apical septum, apical lateral, mid anterolateral and basal anterolateral respectively. The standard for segmental EF is different from that of global EF and segmental EF ≥ 35% has been considered normal[95]. Table 7 shows the distribution of RWMA by 2D echo. About 40% of patients had RWMA in various regions by 2D echo; predominantly, this was in the anterior/septum/apical region. By VVI however, 34 of 49 patients (69.3%) had reduced segmental EF in one or more regions using a cut-off of 35%. The frequency of reduced EF (regional dysfunction) in each region is shown in Table 8.

Table 7. RWMA by 2D Echo (percentages in brackets)

RWMA	Frequency
None	30 (61.2)
Anterior/septum/ apex	15 (30.6)
Inferior/Posterior/lateral	2 (4.1)
Global hypokinesia	2 (4.1)

Table 8. Regional Dysfunction by VVI (percentages in brackets)

Region	Dysfunction
Region 1- Basal inferoseptum	28 (57.1)
Region 2- Mid inferospetum	20 (40.8)
Region 3- Apical septum	22 (44.9)
Region 4- Apical lateral	20 (40.8)
Region 5- Mid anterolateral	19 (38.8)

Region 6- Basal anterolateral	19 (38.8)

Inter-Observer Correlation for measurement of EF by gated SPECT:

The reliability of ejection fraction measured by gated SPECT in this study was tested by looking at the inter-observer variation in the calculation of EF from the SPECT images in 12 randomly selected patients by two independent nuclear physicians. Excellent agreement was seen for measured EF by SPECT (Pearsons correlation coefficient 0.992, p=0.01) between 2 observers, reflecting good reliability of measurement.

Correction Factor for VVI EF:

A regression equation giving the numerical relationship between SPECT EF and VVI EF was obtained from the linear scatter plot. The SPECT EF can be calculated from the VVI EF as given by the equation: EF (SPECT) = EF (VVI) x 0.9 + 21 or approximately VVI (EF) +20. Considering SPECT EF to be the standard in this study, this can be used as a correction factor, using which the “correct EF” can be derived from the EF measured by VVI.

DISCUSSION

In this study we have evaluated the new echocardiographic modality of velocity vector imaging in the assessment of LV systolic function by ejection fraction. Though VVI employs a complex multi-step algorithm, it is practically easy to use and involves only obtaining a good quality image and tracing the endocardial border of the region of interest. The advantage is that the border is then automatically tracked through successive cycles and hence cardiac motion may be delineated with greater accuracy. Measurement of global and regional EF by VVI was found to be simple and feasible enough to be used in routine clinical practice.

There was a positive linear correlation between the EF measured by VVI and the other modalities viz SPECT and 2D echo. This means that as the value of EF measured by SPECT or 2D echo increases, so does that measured by VVI in a proportionate fashion, and vice versa for a fall in the EF. This positive relationship is important as it shows that in a given population, *relative* differences would be reflected well by the new modality even if absolute values are not the same. Thus, in the serial follow up of a patient for example, an improvement or worsening in the EF reflected by gated SPECT or 2D echo would probably be seen on measurement by VVI as well. In other words, the directional trend of EF is the same by all three modalities tested.

However as per the results obtained from this study, EF measured by VVI does not appear to be accurate in terms of the absolute value. The mean EF as measured by VVI (35 ± 12.08%) was significantly less than that measured by either SPECT (54.2 ± 19.51%) or 2D echo (50.3 ± 8.92%). Taken together, the above facts suggest that the current VVI algorithm

systematically underestimates the ejection fraction as compared to gated SPECT or 2D echo.

In addition to showing that this difference is significant in absolute terms, we also analyzed whether it affects classification into different categories of LV dysfunction as this is more likely to directly affect therapy and clinical decision-making. Hence we classified patients by EF into normal, mild, moderate or severe LV dysfunction based on standard American Society of Echocardiography criteria. A significantly greater proportion of patients were classified as having moderate or severe LV dysfunction by VVI EF as compared to SPECT. Thus, the underestimation of EF by VVI is clinically significant.

Analysis of regional function also showed a difference between 2D echo and VVI. While about 40% of the patients had RWMA on assessment by 2D echo, close to 70% of patients had regional dysfunction as evidenced by reduced regional EF in at least one of the six segments studied by VVI. However, an allowance has to be made for the fact that visual estimation by 2D echo is subjective and may not have been accurate enough to pick out milder degrees of hypocontractility which a numerical measure like regional EF would pick up.

As SPECT was used as the gold standard for comparison in this study, reliability of measurement was checked by looking for any variation in measurement between 2 independent observers in 12 randomly selected patients. The inter observer correlation was excellent, showing that measurement error was not likely to be a significant issue in calculating EF from gated SPECT. As mentioned previously, assessment of LV function by gated SPECT is a well accepted modality which has been validated against other techniques of LV function measurement[93]. Hence its use in this study as the standard is justified and lends credence to the observed results.

Finally, we looked at the numerical relationship between the calculated VVI EF and SPECT EF and found by regression equation that the VVI EF was numerically about 20 less than the SPECT EF. In other words, the “correct” (SPECT) EF can be known by adding 20 to the VVI EF. This can be incorporated as a correction factor in the VVI algorithm to improve its accuracy. This will need to be prospectively validated.

It is difficult to speculate as to why there was a significant error in the EF measured by VVI. The software is automated and the role of the echocardiographer is limited to only tracing the endocardial border, making operator related error unlikely. To the best of our knowledge, this is the first study to attempt to validate EF measured by VVI against an existing standard. Studies assessing VVI in the clinical setting are sparse at present. Chen et al studied the use of VVI in a small number of post myocardial infarction patients by measuring strain, strain rate and segmental EF. They found that these parameters were significantly lower in infarct segments than in the corresponding segments of the normal controls. There was good correlation between the strain measured by VVI and that measured by tissue Doppler. Inter and intraobserver variability in the VVI measurements was 4.6% and 7% respectively. They concluded that VVI could be a useful tool in measuring regional myocardial systolic function[95]. Vannan et al., in a case report have described the measurement of strain using VVI in a patient undergoing CRT. They showed that although longitudinal and radial velocities of the LV were synchronized after CRT, VVI showed a persistent heterogeneity of circumferential strain[8]. Thus, VVI could possibly be a better tool for assessing the outcome of CRT by better measuring the circumferential and radial dynamics of the LV, which are components of the torsional deformation of the LV described earlier.

As VVI is a new and still evolving technology, the software and tracking algorithm may need

to be “fine tuned” as data from more clinical studies become available. There is no doubt that VVI is a conceptually sound technology with good future potential and further trials will help delineate any possible sources of error which can then be addressed.

In conclusion, measurement of ejection fraction by VVI is simple and feasible for use in clinical practice. This study showed a positive linear correlation between EF measured by VVI, gated SPECT and 2D echo. However, VVI significantly underestimated EF in comparison to gated SPECT and 2D echo by a magnitude that was clinically relevant in classifying patients into categories of LV dysfunction. This could be due to as yet unknown technical factors in the tracking algorithm. A correction factor was calculated which can be incorporated into the VVI algorithm to improve its accuracy.

LIMITATIONS

1. The number of patients studied was limited and hence the findings need to be confirmed in a larger population.

2. The patients studied are a heterogeneous population in terms of LV function and whether any variations exist in the measurement of EF by VVI in different subsets of patients cannot be adequately commented upon due to the limited numbers studied. However, in the current study, the relationship between VVI and SPECT EF appeared to be uniform irrespective of underlying pathology and extent of LV dysfunction.

3. This study looked only at ejection fraction; the possible contribution of other techniques like strain and strain rate imaging by VVI was not addressed.

SUMMARY OF MAIN FINDINGS

1. VVI is an easy to use technology from which global and regional EF can be calculated.

2. The mean ejection fraction (EF) calculated by VVI was 35 ± 12.08%, as compared to 54.2 ± 19.51% by SPECT ($p<0.001$ vs. VVI) and 50.3 ± 8.92% with 2D echo ($p<0.001$ vs. VVI). The mean EF measured by VVI was significantly less than that measured by the other modalities.

3. There was a positive linear correlation between the VVI EF and SPECT EF (correlation coefficient 0.577; $p=0.01$) as well as 2D EF (correlation coefficient 0.573; $p=0.01$).

4. Significantly greater proportion of patients were categorized as having moderate or severe LV dysfunction by VVI (75.5%) when compared to SPECT (34.7%) or 2D echo (32.7%).

5. There was excellent inter-observer correlation for EF measured by SPECT.

6. A correction factor was derived from the regression equation for VVI EF as follows: EF (SPECT) = EF (VVI) x 0.9 + 21 or approximately VVI (EF) +20.

BIBLIOGRAPHY

1. Wang TJ, Evans JC, Benjamin EJ, et al. Natural history of asymptomatic left ventricular systolic dysfunction in the community. Circulation 2003; 108:977–82

2. Rihal CS, Davis KB, Kennedy JW, et al. The utility of clinical, electrocardiographic, and roentgenographic variables in the prediction of left ventricular function. Am J Cardiol 1995;75:220–3.

3. Curtis JP, Sokol SI, Wang Y, et al: The association of left ventricular ejection fraction, mortality, and cause of death in stable outpatients with heart failure. J Am Coll Cardiol 2003; 42:736–42

4. Dittoe N; Stultz D; Schwartz BP et al. Quantitative left ventricular systolic function: From chamber to myocardium. Crit Care Med 2007; 35[Suppl.]:S330–9.

5. Hundley W, Kizilbash A, Afridi I, et al: Administration of an intravenous perfluorocarbon contrast agent improves echocardiographic determination of left ventricular volumes and ejection fraction: Comparison with cine MRI. J Am Coll Cardiol 1998; 32: 1426–32

6. Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). Circulation. 2005; 112 (12):e154-235.

7. Bohs LN, Trahey GE: A novel method for angle independent ultrasonic imaging of blood flow and tissue motion. IEEE Trans Biomed Eng.1991; 38:280-6.

8. Vannan MA, Pedrizzetti G, Li P et al. Effect of Cardiac Resynchronization Therapy on

Longitudinal and Circumferential Left Ventricular Mechanics by Velocity Vector Imaging: Description and Initial Clinical Application of a Novel Method Using High-Frame Rate B-Mode Echocardiographic Images. Echocardiography 2005; 22:826-30.

9. Wyatt HL, Heng MK, Meerbaum S, et al. Cross-sectional echocardiography II. Analysis of mathematic models for quantifying volume of the formalin-fixed left ventricle. Circulation 1980;61:1119–25.

10. Opie LH. Mechanisms of cardiac contraction and relaxation. *In* Libby P, Bonow R, Mann D, Zipes DP, editors. Braunwald's Heart Disease. A textbook of Cardiovascular Medicine 8th ed. Philadelphia, Elsevier Saunders, 2008: 509-39.

11. Allen, D. G., J. C. Kentish. The cellular basis of the length–tension relation in cardiac muscle. J. Mol. Cell. Cardiol. 1985.17:821–40.

12. Huwez FU, Houston AB, Watson J et al: Age and body surface related normal upper and lower limits of M mode echocardiographic measurements and left ventricular volume and mass from infancy to early adulthood. Br Heart J 1994; 72(3):276-80.

13. Ross J Jr. Afterload mismatch and preload reserve: A conceptual framework for the analysis of ventricular function. Prog Cardiovasc Dis 1976; 18:255–64.

14. Nixon JV, Murray RG, Leonard PD, et al: Effect of large variations in preload on left ventricular performance characteristics in normal subjects. Circulation 1982; 4:698–703.

15. Feigenbaum H, Armstrong W, Ryan T. Evaluation of systolic and diastolic function of the left ventricle. *In* Feigenbaum's Echocardiography. 6th ed. Philadelphia, Lippincott Williams & Wilkins, 2005: 138-80.

16. Lang RM, Bierig M, Devereux RB, et al: Recommendations for chamber quantification. Eur J Echocardiogr 2006, 7:79 -108.

17. Foster E, Cahalan MK. The search for intelligent quantitation in echocardiography: ‘‘eyeball,’’ ‘‘trackball’’ and beyond. J Am Coll Cardiol

1993;22:848–50.

18. T H Marwick. Techniques for comprehensive two dimensional echocardiographic assessment of left ventricular systolic function. Heart 2003;89(Suppl III):iii2–8.

19. Stamm RB, Carabello BA, Mayers DL, et al. Two-dimensional echocardiographic measurement of left ventricular ejection fraction: prospective analysis of what constitutes an adequate determination. Am Heart J 1982;104:136–44

20. Malhotra V, Nwogu J, Bondmass MD, et al: Is the technically limited echocardiographic study an endangered species? Endocardial border definition with native tissue harmonic imaging and Optison contrast. A review of 200 cases. J Am Soc Echocardiogr 2000; 13:771–3.

21. Mulvagh SL, DeMaria AN, Feinstein SB, et al: Contrast echocardiography: Current and future applications. J Am Soc Echocardiogr 2000; 13:331–42.

22. Malm S, Frigstad S, Sagberg E, et al: Accurate and reproducible measurement of left ventricular volume and ejection fraction by contrast echocardiography: A comparison with MRI. J Am Coll Cardiol 2004; 44: 1030–35.

23. Yvorchuk KJ, Davies RA, Chan KL: Measurement of left ventricular ejection fraction by acoustic quantification and comparison with radionuclide angiography. Am J Cardiol 1994; 74:1052–56.

24. Bednarz J, Vignon P, Mor-Avi V, et al: Color kinesis: Principles of operation and technical guidelines. Echocardiography 1998; 15: 21–34.

25. Mock MB, Ringqvist I, Fisher LD, et al: Survival of medically treated patients in the Coronary Artery Surgery Study (CASS) registry. Circulation 1982; 66:562–8.

26. Sharir T, Germano G, Kavanagh PB, et al: Incremental prognostic value of post-stress left ventricular ejection fraction and volume by gated myocardial perfusion single photon emission computed tomography. Circulation 1999; 100:1035–42.

27. Ross J Jr: Afterload mismatch in aortic and mitral valve disease: Implications for surgical therapy. J Am Coll Cardiol 1985; 5:811–26.

28. Cohn JN, Ferrari R, Sharpe N: Cardiac remodeling: Concepts and clinical implications. A consensus paper from an international forum on cardiac remodeling. Behalf of an International Forum on Cardiac Remodeling. J Am Coll Cardiol 2000; 35: 569–82.

29. Sanderson JE, Fraser AG. Systolic Dysfunction in Heart Failure with a Normal Ejection Fraction: Echo-Doppler Measurements. Prog Cardiovasc Dis 2006, 49(3):196-206.

30. Hung J, Lang R, Flachskampf F et al. 3D Echocardiography: A Review of the Current Status and Future Directions. J Am Soc Echocardiogr, 2007, 20(3):213-33.

31. Hibberd MG, Chuang ML, Beaudin RA, et al. Accuracy of three dimensional echocardiography with unrestricted selection of imaging planes for measurement volumes and ejection fraction. Am Heart J 2000;140:469-75.

32. Sugeng L, Mor-Avi V, Weinert L, et al: Quantitative assessment of left ventricular size and function: Side-by-side comparison of real- time three-dimensional echocardiography and computed tomography with magnetic resonance reference. Circulation 2006; 114: 654–61.

33. Fujimoto S, Mizuno R, Nakagawa Y et al. Estimation of the right ventricular volume and ejection fraction by transthoracic three-dimensional echocardiography: a validation study using magnetic resonance imaging. Int J Card Imaging 1998;14:385-90.

34. Nishimura RA, Reeder GS, Miller FA, et al. Prognostic value of predischarge 2-dimensional echocardiogram after acute myocardial infarction. Am J Cardiol 1984;53:429–32.

35. Kolias TJ, Aaronson KD, Armstrong WF. Doppler-derived dP/dt and - dP/dt predict survival in congestive heart failure. J Am Coll Cardiol 2000; 36:1594–99.

36. Pai RG, Bansal RC, Shah PM: Doppler derived rate of left ventricular pressure rise: Its correlation with the postoperative left ventricular function in mitral regurgitation. Circulation

1990; 82:514–20.

37. Tei C, Ling LH, Hodge DO, et al: New index of combined systolic and diastolic myocardial performance: A simple and reproducible measure of cardiac function: A study in normals and dilated cardiomyopathy. J Cardiol 1995; 26:357–66.

38. Tei C, Nishimura RA, Seward JB, et al. Noninvasive Doppler-derived myocardial performance index: correlation with simultaneous measurements of cardiac catheterization measurements. J Am Soc Echocardiogr 1997;10:169–78.

39. Miller D, Farah MG, Liner A, et al: The relation between quantitative right ventricular ejection fraction and indices of tricuspid annular motion and myocardial performance. J Am Soc Echocardiogr 2004; 17:443–7.

40. Reichek N, Wilson J, St John SM, et al. Noninvasive determination of left ventricular end-systolic stress: validation of the method and initial application. Circulation 1982;65:99–108.

41. Gaasch WH, Zile MR, Hoshino PK, et al. Stress-shortening relations and myocardial blood flow in compensated and failing canine hearts with pressure-overload hypertrophy. Circulation 1989;79:872–83.

42. Vinereanu D, Khokhar A, Fraser AG: Reproducibility of pulsed wave tissue Doppler echocardiography. J Am Soc Echocardiogr 1999; 12:492–9.

43. Sanderson JE, Wang M, Yu CM. Tissue Doppler imaging for predicting outcome in patients with cardiovascular disease. Curr Opin Cardiol 2004;19:458–63.

44. Henein MY, Gibson DG. Long axis function in disease. Heart 1999;81:229–31.

45. Pai RG, Bodenheimer MM, Pai SM et al. Usefulness of systolic excursion of the mitral annulus as an index of left ventricular systolic function. Am J Cardiol 1991;67:222– 4.

46. Alam M, Wardell J, Andersson E et al. Effects of first myocardial infarction on left ventricular systolic and diastolic function with the use of mitral annular velocity determined by pulsed wave Doppler tissue imaging. J Am Soc Echocardiogr 2000;13:343–52.

47. Sanderson JE. Heart failure with a normal ejection fraction. Heart 2007;93:155– 8.

48. Fang ZY, Leano R, Marwick TH. Relationship between longitudinal and radial contractility in subclinical diabetic heart disease. Clin Sci (Lond) 2004;106:53– 60.

49. Nagueh SF, Bachinski LL, Meyer D, et al. Tissue Doppler imaging consistently detects myocardial abnormalities in patients with hypertrophic cardiomyopathy and provides a novel means for an early diagnosis before and independently of hypertrophy. Circulation 2001; 104:128 –30.

50. Nagueh SF, Sun H, Kopelen HA et al. Hemodynamic determinants of the mitral annulus diastolic velocities by tissue Doppler. J Am Coll Cardiol 2001;37:278–85.

51. Sohn DW, Chai IH, Lee DJ, et al. Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function. J Am Coll Cardiol 1997;30:474–80.

52. Nagueh SF, Middleton KJ, Kopelen HA et al. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. J Am Coll Cardiol 1997;30:1527–33.

53. Ommen SR, Nishimura RA, Appleton CP, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. Circulation 2000;102:1788 –94.

54. Hillis GS, Moller JE, Pellikka PA, et al. Noninvasive estimation of left ventricular filling pressure by E/E' is a powerful predictor of survival after acute myocardial infarction. J Am Coll Cardiol 2004;43:360 –7.

55. Rihal CS, Nishimura RA, Hatle LK et al. Systolic and diastolic dysfunction in patients with clinical diagnosis of dilated cardiomyopathy. Relation to symptoms and prognosis. Circulation 1994;90:2772–9.

56. Wang M, Yip GW, Wang AY, et al. Peak early diastolic mitral annulus velocity by tissue Doppler imaging adds independent and incremental prognostic value. J Am Coll Cardiol 2003;41:820–6.

57. Marwick TH, Case C, Leano R, et al. Use of tissue Doppler imaging to facilitate the prediction of events in patients with abnormal left ventricular function by dobutamine echocardiography. Am J Cardiol 2004;93:142– 6.

58. Yu CM, Lin H, Zhang Q et al. High prevalence of left ventricular systolic and diastolic asynchrony in patients with congestive heart failure and normal QRS duration. Heart 2003;89:54–60.

59. Yu CM, Fung JWH, Lin H et al. Predictors of left ventricular reverse remodeling after cardiac resynchronization therapy for heart failure secondary to idiopathic dilated or ischemic cardiomyopathy. Am J Cardiol 2003;91:684-8.

60. Cho GY, Song JK, Park WJ, et al. Mechanical dyssynchrony assessed by tissue Doppler imaging is a powerful predictor of mortality in congestive heart failure with normal QRS duration. J Am Coll Cardiol 2005; 46:2237– 43.

61. Mele D, Pasanisi G, Capasso F, et al. Left intraventricular myocardial deformation dyssynchrony identifies responders to cardiac resynchronization therapy in patients with heart failure. Eur Heart J 2006; 27: 1070–8.

62. Heimdal A, Stoylen A, Torp H et al. Real-time strain rate imaging of the left ventricle by ultrasound. J Am Soc Echocardiogr 1998;11:1013–9.

63. Sun JP, Popovic ZB, Greenberg ML, et al: Noninvasive quantification of regional myocardial function using Doppler-derived velocity, displacement, strain rate, and strain in healthy volunteers: Effects of aging. J Am Soc Echocardiogr 2004; 17:132–8.

64. Gilman G, Khandheria BK, Hagen ME, et al: Strain rate and strain: A step-by-step approach in image and data acquisition. J Am Soc Echocardiogr 2004; 17:1011–20.

65. Urheim S, Edvardsen T, Torp H et al. Myocardial strain by Doppler echocardiography. Validation of a new method to quantify regional myocardial function. Circulation 2000; 102:1158–64.
66. Edvardsen T, Gerber BL, Garot J et al. Quantitative assessment of intrinsic regional myocardial deformation by Doppler strain rate echocardiography in humans: validation against 3-dimensional tagged magnetic resonance imaging. Circulation 2002;106:50–6.
67. Hoffmann R, Altiok E, Nowark, et al: Strain rate measurements by Doppler echocardiography allows improved assessment of myocardial viability in patients with depressed left ventricular function. J Am Coll Cardiol 2002; 39:443–9.
68. Voigt JU, Exner B, Schmiedehausen K, et al: Strain-rate imaging during dobutamine stress echocardiography provides objective evidence of inducible ischemia. Circulation 2003; 107:2120–6
69. Park TH, Nagueh SF, Khoury DS, et al. Impact of myocardial structure and function postinfarction on diastolic strain measurements: implications for assessment of myocardial viability. Am J Physiol Heart Circ Physiol 2006;290:H724–31.
70. Sutherland GR, Di SG, Claus P, et al. Strain and strain rate imaging: a new clinical approach to quantifying regional myocardial function. J Am Soc Echocardiogr 2004;17:788–802.
71. Mottram PM, Haluska B, Leano R, et al. Effect of aldosterone antagonism on myocardial dysfunction in hypertensive patients with diastolic heart failure. Circulation 2004;110:558–65.
72. Weidemann F, Jamal F, Kowalski M, et al: Can strain rate and strain quantify changes in regional systolic function during dobutamine infusion, β -blockade and atrial pacing-implications for quantitative stress echocardiography. J Am Soc Echocardiogr 2002; 15:416–24.
73. Leitman M, Lysyansky P, Sidenko S, et al: Two dimensional strain-a novel software for

real-time quantitative echocardiographic assessment of myocardial function. J Am Soc Echocardiogr 2004;17:1021-9.

74. Smith SW, Trahey GE, Hubbard SM, et al: Properties of acoustical speckle in the presence of phase aberration. Part II: Correlation lengths. Ultrason Imaging 1988;10:29-51.

75. Helle-Valle T, Crosby J, Edvardsen T, et al: New noninvasive method for assessment of left ventricular rotation: Speckle tracking echocardiography. Circulation 2005;112:3149-3156.

76. Amundsen BH, Helle-Valle T, Edvardsen T, et al: Noninvasive myocardial strain measurement by speckle tracking echocardiography: Validation against sonomicrometry and tagged magnetic resonance imaging. J Am Coll Cardiol 2006;47:789-93.

77. Cho GY, Chan J, Leano R, et al: Comparison of two-dimensional speckle and tissue velocity based strain and validation with harmonic phase magnetic resonance imaging. Am J Cardiol, 2006; 97:1661-6.

78. Suffoletto MS, Dohi K, Cannesson M, et al: Novel -speckle-tracking radial strain from routine black-and-white echocardiographic images to quantify dyssynchrony and predict response to cardiac resynchronization therapy. Circulation 2006;113:960-8.

79. Jackson J, Houle H. Velocity Vector Imaging- White Paper. Ultrasound division, Siemens Medical Solutions USA, Inc.

80. Cannesson M, Tanabe M, Suffoletto MS, et al. Velocity vector imaging to quantify ventricular dyssynchrony and predict response to cardiac resynchronization therapy. Am J Cardiol. 2006;98:949-53.

81. Notomi Y, Lysyansky P, Setser RM, et al: Measurement of ventricular torsion by two-dimensional ultrasound speckle tracking imaging. J Am Coll Cardiol 2005;45:2034- 41.

82. Friedberg MK, Silverman NH, Dubin AM, et al. Right ventricular mechanical dyssynchrony in children with hypoplastic left heart syndrome. : J Am Soc Echocardiogr. 2007;20:1073-9

83. Lima JAC, Desai MY. Cardiovascular Magnetic Resonance Imaging: Current and

Emerging Applications. J Am Coll Cardiol 2004;44:1164 –71.

84. Constantine G, Shan K, Flamm SD, et al. Role of MRI in clinical cardiology. Lancet 2004; 363: 2162–71.

85. Escolar E, Weigold G, Fuisz A, et al. New imaging techniques for diagnosing coronary artery disease. CMAJ 2006;174:487-95.

86. Rademakers FE, Bogaert J. Cardiac Dysfunction in Heart Failure with Normal Ejection Fraction: MRI measurements. Prog Cardiovasc Dis, 2006; 49: 215-27.

87. Raman SV, Shah M, McCarthy B, et al. Multi–detector row cardiac computed tomography accurately quantifies right and left ventricular size and function compared with cardiac magnetic resonance. Am Heart J. 2006;151:736-44

88. Schlosser T, Mohrs OK, Magedanz A, et al. Assessment of left ventricular function and mass in patients undergoing computed tomography (CT) coronary angiography using 64-detector-row CT: comparison to magnetic resonance imaging. Acta Radiol. 2007;48:30-5.

89. Abbara S, Chow BJ, Pena AJ, et al. Assessment of left ventricular function with 16- and 64-slice multi-detector computed tomography. : Eur J Radiol. 2007; Sep 7 [Epub ahead of print].

90. Fine JJ, Hopkins CB, Ruff N, et al. Comparison of Accuracy of 64-Slice Cardiovascular Computed Tomography with Coronary Angiography in patients with suspected coronary artery disease. Am J Cardiol 2006;97:173–4.

91. Zaret BL, Wackers FJ, Terrin ML, et al. Value of radionuclide rest and exercise left ventricular ejection fraction in assessing survival of patients after thrombolytic therapy for acute myocardial infarction: results of thrombolysis in myocardial infarction (TIMI) phase II study. The TIMI study group. J Am Coll Cardiol 1995;26:73–9.

92. Griffin BP, Shah PK, Diamond GA, et al. Incremental prognostic accuracy of clinical,

radionuclide and hemodynamic data in acute myocardial infarction. Am J Cardiol 1991;68:707–12.

93. Sciagra' R, Leoncini M. Gated single-photon emission computed tomography The present-day "one-stop-shop" for cardiac imaging. Q J Nucl Med 2005;49:19-29.

94. Lang RM, Bierig M, Devereux RB, et al: Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005; 18:1440–63.

95. Chen J, Cao T, Duan Y, et al. Velocity Vector Imaging in Assessing the Regional Systolic Function of Patients with Post Myocardial Infarction. Echocardiography 2007, 24: 940-5.

Proforma

ASSESSMENT OF LV SYSTOLIC FUNCTION BY VELOCITY VECTOR IMAGING

1. Name: 2. Age/sex: 3. Hosp.No:

4. Risk Factors: Diabetes: yes/no
Hypertension: yes/no
Smoker : yes/no
Dyslipidemia: yes/no
Family history: yes/no

5. Symptoms: Angina: yes/no
Dyspnea: yes/no
Orthopnea: yes/no
PND : yes/no
Palpitations: yes/no
Syncope: yes/no
Fatigue : yes/no

6. NYHA Class: I/ II/ III/ IV

7. Previous STEMI: yes/no

If Yes, site: Anteroseptal
Extensive anterior
Lateral
Inferior
Large Inferior (Inferoposterior +/- RVMI)

Thrombolysed: yes/no/not known

8. Previous ACS (other than STEMI): yes/no

9. ECG: Q Infarct: yes/no
LBBB : yes/no

10. Chest X Ray: Cardiomegaly: yes/no (CTR-)

11. Ejection Fraction:

By 2D Echo: Global-
RWMA-

By Gated SPECT:

By VVI : Global-
Regional- 1. 2. 3. 4. 5. 6.

12. Sestamibi Results: Normal
Fixed Defect Region:
Ischemia Region:

13. Coronary Angiogram: Not Done
SVD
DVD
TVD
LMD

LV Angio Normal
LV Dysfunction RWMA-
Hypercontractile LV

12. Drugs: Aspirin: yes/no
Beta blockers: yes/no
Statin: yes/no Dose: 10/ 20/ 40
ACEI/ARB: yes/no
Nitrate: yes/no

GLOSSARY FOR MASTER CHART

hospno	- Hospital number
dm	- Diabetes mellitus
htn	- Hypertension
sm	- Smoking
dyslip	- Dyslpidemia
famhis	- Family History
orthop	- Orthopnea
pnd	- Paroxysmal nocturnal dyspnea
palpit	- Palpitations
nyha	- New York Heart Association functional class
stemi	- ST elevation myocardial infarction
misite	- Site of STEMI
thrombol	- Thrombolysis done (NA = not applicable)
acs	- Acute coronary syndrome (other than STEMI)
qinfar	- Q infarct on ECG
lbbb	- Left Bundle Branch Block on ECG
cmegaly	- Cardiomegaly on chest X-ray
ctr	- Cardiothoracic ratio (%)
twodef	- Ejection fraction by 2D echo
twodlvd	- LV dysfunction by 2D echo twocat2d

- LV dysfunction by 2D echo in 2 categories	
twodrwma	- RWMA by 2D echo (nil = no RWMA)
spectef	- Ejection fraction by gated SPECT
intero	- SPECT EF by 2nd independent observer in 12 cases
spectlvd	- LV dysfunction by SPECT
spelvtwo	- LV dysfunction by SPECT in 2 categories
vvief	- Ejection fraction by VVI
vvilvd	- LV dysfunction by VVI
vvilvtwo	- LV dysfunction by VVI in 2 categories
vvireg1 to 6	- Segmental EFs in regions 1 to 6 by VVI
sestamib	- Ischemia by SPECT
cag	- Coronary angiogram minor = minor disease SVD = Single vessel disease DVD = Double vessel disease TVD = Triple vessel disease LM = Left main disease
lvangio	- LV angiogram
rwmalvan	- RWMA by LV angio (NA = not available)
betabloc	- Beta blocker use

acei	- ACE inhibitor/ ARB use
lvdreg 1-6	-LV dysfunction by reduced segmental EF in regions 1 to 6 by VVI