"UTILITY VALUE OF TISSUE DOPPLER IMAGING DURING DOBUTAMINE STRESS IN DIFFERENTIATING ISCHEMIC FROM NONISCHEMIC DILATED CARDIOMYOPATHY"

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CERTIFICATE

This is to certify that the dissertation entitled **"UTILITY VALUE OF TISSUE DOPPLER IMAGING DURING DOBUTAMINE STRESS IN DIFFERENTIATING ISCHEMIC FROM NONISCHEMIC DILATED CARDIOMYOPATHY"** is the bonafide original work of **Dr.C.ARUMUGAM**, in partial fulfillment of the requirements for D.M. Branch-II (CARDIOLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2007.The period of post-graduate study and training was from August 2004 to July 2007.

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DECLARATION

I **Dr.C.ARUMUGAM,** solemnly declare that this dissertation entitled, **UTILITY VALUE OF TISSUE DOPPLER IMAGING DURING DOBUTAMINE STRESS IN DIFFERENTIATING ISCHEMIC FROM NONISCHEMIC DILATED CARDIOMYOPATHY"** is a bonafide work done by me at the department of Cardiology,Madras Medical College and Government General Hospital during the period 2004 – 2007 under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital,Professor V.Jaganathan M.D.D.M.This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical university,towards partial fulfillment of requirement for the award of **D.M. Degree (Branch-II) in Cardiology.**

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CONTENTS

ABBREVIATIONS

TDI	Tissue Doppler Imaging
CAD	Coronaty Artery Disease
DCM	Dilated Cardiomyopathy
2DE	Two Dimensional Echocardiography
LV	Left Ventricle
RWMA	Regional Wall Motion Abnormalities
DSE	Dobutamine Stress Echocardiography
PET	Positron Emission Tomography
EBCT	Electron Beam Computed Tomography
CMR	Cardiovascular Magnetic Resonance
MRI	Magnetic Resonance Imaging
PWTD	Pulsed-Wave Tissue Doppler
TA	Total Amplitude
PES	Postejection shortening
SA	Systolic amplitude
LVEF	Left Ventricular Ejection Fraction
RVEF	Right Ventricular Ejection Fraction
WHO	World Health Organization
MI	Myocardial Infarction
ECG	Electrocardiogram

ABBREVIATIONS…

LVIDd	Left Ventricular Internal Dimension at end-diastole
LVIDs	Left Ventricular Internal Dimension at end-systole
SPECT	Single-Photon Emission Computed Tomography
CC	Coronary Calcification
MAC	Mitral Anular Calcification
AVC	Aortic Valve Calcification
TAC	Thoracic Aortic Calcification
CAS	Coronary Artery Stenosis
S’	Systolic velocity
Ea or E’	Early diastolic velocity
Aa or A’	Late diastolic velocity
LBBB	Left Bundle Branch Block
WMSI	Wall Motion Score Index
NYHA	New York Heart Association
LAD	Left Anterior Descending coronary artery

"learn to heal"

INTRODUCTION

Differentiating ischemic from nonischemic cardiomyopathy poses a particular problem, but this is important prognostically and therapeutically. Patients with ischemic cardiomyopathy have worse prognosis than the patients with idiopathic dilated cardiomyopathy. Joseph et al, in 1983 have demonstrated that in patients with severe chronic left ventricular failure, mortality rate in patients with coronary artery was 46% and 69% at 1 and 2 years, respectively compared with 23% and 48% at 1 and 2 years in those with idiopathic dilated cardiomyopathy [1]. In 1997, Bradley and colleagues also have shown ischemic etiology is a significant independent predictor of mortality in patients with cardiomyopahy [2].

Therapeutically also it is important to distinguish between ischemic and nonischemic cardiomyopathy because the diagnosis influences the management. Antiplatelets and lipid lowering therapy are important in management of patients with cardiomyopathy of ischemic etiology. Revascularisation in patients with low ejection fraction and significant coronary artery disease is strongly associated with improved survival [3-5] and should be considered in all patients with ischemic cardiomyopathy and proven hibernation. Moreover ischemic cardiomyopathy may not respond to medical therapy as favorably as patients with nonischemic cardiomyopathy.

Differentiating ischemic from nonischemic cardiomyopathy clinically is not always easy. Although ischemic cardiomyopthy is generally a late consequence of clinically established coronary artery disease, sometimes the clinical course is really occult and indistinguishable from idiopathic cardiomyopathy. An ischemic cause is probable in patients with history of definite or documented prior myocardial infarction or left ventricular aneurysm in echocardiogram [6,7]. However, some patients with ischemic cardiomyopathy have neither history nor electrocardiographic

evidence of myocardial infarction [8],never complaint of chest pain [9] and shows diffuse rather than regional hypocontractility [6,10]. Conversely many patients with idiopathic dilated cardiomyopathy report frequent episodes of chestpain [11] and have electrocardiographic evidence of myocardial infarction [12].

Appropriate differentiation of these two cardiomyopathy is achieved by coronary angiography since it remains the gold standard test to identify coronary artery disease, but coronary angiogram is an invasive method with its attendant risks so a noninvasive method would be preferable which may decrease the unnecessary risk, cost and inconvenience associated with cardiac catheterization. Unfortunately most of the currently used noninvasive methods to distinguish the etiology of left ventricular dysfunction have been of limited value [13] and many non-invasive techniques have been tested with variable accuracy [14,15,16,17,18,19]. There are some limitations in interpretation and availability of these tests while inconsistent findings have been reported. The relatively low specificity and predictive value of these tests which are further reduced with more pronounced left ventricular dysfunction often preclude definitive clinical decisions in individual cases.

Ischemic cardiomyopthy may be suspected on the basis of **clinical and electrocardiographic data**. However, the sensitivity and specificity of these data are often inadequate for individual patient management decisions [20,21,22,23,24] and further confounded by the frequent presence of a nondiagnostic electrocardiography with conduction abnormalities [24] and high prevalence of asymptomatic myocardial infarction [8].**Exercise stress testing** is the standard noninvasive technique used for detection of coronary artery disease in patients without significant left ventricular dysfunction or dilated cardiomyopathy, but it is not being used for diagnostic purpose in patients with dilated heart and left ventricular dysfunction because of their reduced ability patients to perform

dynamic stress. Additionally frequent presence of electrocardiographic conduction abnormalities in these group of patients at rest impairs interpretation of stress electrocardiography.

The detection of **regional wall motion abnormalities at rest** by echocardiography or ventriculography (contrast or radionuclide) is often thought to be a reliable indicator of presence of significant coronary artery disease obstruction and prior myocardial infarction [25-27], but Robert et al [6] demonstrated that resting regional wall motion abnormalities detect significant coronary artery disease with high specificity in patients with normal sized ventricle but has low specificity in patients with dilated ventricles. Moreover regional wall motion abnormalities at rest have been demonstrated in as many as two thirds of patients with nonischemic cardiomyopathy whereas patients with ischemic cardiomyopathy might have uniform hypokinesia [6]. So resting regional wall motion abnormalities do not reliably distinguish ischemic from nonischemic cardiomyopathy.

Dobutamine stress echocardiography is an accurate noninvasive technique for evaluating coronary artery disease in nondilated heart with sensitivity and specificities in the range of 80-85% [26], but only limited data available about the role of dobutamine stress echocardiography in detection of coronary artery disease in dilated cardiomyopathy which had been done in small number of patients. Moreover adequate training is required to obtain these impressive results [29].Also the lack of uniform diagnostic criteria is a significant limitation in the agreement of even expert readers, especially in situations of poor imaging quality and subtle wall motion abnormalities. The fundamental problem underlying both of these limitations is the subjective nature of stress echocardiography. Also presence of left bundle branch block which is being

common in dilated cardiomyopathy patients further impair the wall motion analysis during stress echocardiography.

Several other noninvasive techniques such as right ventricular function, coronary echocardiography, resting thallium-201 myocardial perfusion scanning, positron emission tomography(PET), coronary calcium score using electron beam computed tomography(EBCT), carotid scanning for measuring carotid atherosclerosis have been used to distinguish these two forms of cardiomyopathy, but distinction has been limited by controversial findings.

Right ventricular function — The right ventricular ejection fraction (RVEF) has been proposed as a means of distinguishing between ischemic and nonischemic cardiomyopathies. Ischemia and infarction usually spare the right ventricle; as a result, patients with an ischemic cardiomyopathy should have a relatively normal RVEF. In contrast, a nonischemic cardiomyopathy is a global process that should involve the right ventricle and should be associated with a reduced RVEF. Once again, this theoretical distinction has limited clinical utility [43,44]. In one series of 23 patients with idiopathic cardiomyopathy and 36 patients with ischemic cardiomyopathy, the mean RVEF was, as expected, lower in patients with a nonischemic cardiomyopathy (31% versus 45% for those with an ischemic cardiomyopathy)[43]. However, there was considerable overlap between the two groups: 22 percent of patients with a nonischemic cardiomyopathy had a normal RVEF, while 34 percent of patients with an ischemic cardiomyopathy had a reduced RVEF[43]. In another study of 76 patients with proven nonischemic cardiomyopathy, 54 percent had normal RVEF in the presence of reduced LVEF [44].

Transthoracic coronary echocardiography was used in one study to distinguish ischemic from nonischemic cardiomyopathy on the basis of

visualization of coronary arteries, but it is not possible to visualize coronary arteries in all patients by transthoracic echocardiogram, and also only proximal coronaries can be visualized. **Thallium scintigraphy** has been used in differentiation of ischemic from nonischemic cardiomyopathy, but it gives false-positive anteroseptal and septal perfusion defects in patients with left bundle branch block [30].**Positron emission tomography(PET)** has also been shown to been useful to identify ischemic etiology in patients with dilated cardiomyopathy, but is limited by its availability and expense.

A number of authors have proposed that the development of a user-friendly quantitative approach should overcome the limitations of the subjective evaluation of dobutamine stress echocardiography images [31,32] and other currently used techniques. Several investigators have shown **Tissue Doppler Imaging(TDI)**, a novel echocardiographic method that measures the **long axis function** of the ventricles quantitatively, to be a sensitive alternative to the present echocardiographic and scintigraphic imaging techniques to evaluate stress tests [33,34].Quantification of myocardial function by Pulsed Doppler myocardial imaging during dobutamine stress have also been demonstrated to be a feasible, accurate, and reproducible technique [34].

Left ventricular fibres are predominantly arranged longitudinally or obliquely in the subendocardium and subepicardium and circumferentially in the intermediate layers. During early systole, the longitudinal and oblique fibres begin to contract first causing the long-axis to shorten and the left ventricular cavity to become more spherical. After a mean delay of 25 ms the circumferential fibres also begin to contract, and throughout the rest of systole both circumferential and longitudinal axes contract synchronously [33]. This normal pattern is disrupted early in coronary artery disease as subendocardial longitudinal fibres are more sensitive to ischemia [34] than circumferential fibres.

Therefore abnormalities of long axis function may be of practical use as indicators of ischemia during stress testing [35]. Furthermore stress induced changes in long axis function can be measured objectively [36,37].

By studying left ventricular long axis function by simple M-mode echocardiography, Mishra et al reported that the normal increase in systolic amplitude of mitral annulus occurring with dobutamine administration is attenuated in patients with coronary artery disease and normal left ventricular dimension [38]. Simonson and Schiller [39] showed that a reduction in long axis function, called descent of the base in their study, correlated well with impaired left ventricular ejection fraction in a large group of patients including those with coronary artery disease. Gibson's group [22] confirmed that, in patients with ischaemic disease, long-axis shortening was delayed to 85 ms after the Q wave from a normal mean of 55 ms, along with a reduction in the amplitude of long axis shortening. Similar results were found by Henein *et al*.[40] who further showed that these abnormalities resolved after successful angioplasty. This suggested that longaxis function might be useful for the detection of ischaemia. Alam and associates [35] assessed long axis shortening before and after bicycle exercise and found that there was a blunted increase of long axis shortening in patients with coronary artery disease. They used an upper limit of normal of 3 mm based on inter-observer variability. This gave a sensitivity of 76% for the detection of angiographically significant coronary artery disease and of 88% for the detection of reversible ischaemia on thallium stress imaging. However, the sensitivity was only 50% for single vessel disease. Based on the above observations Duncan and co-workers used left ventricular long axis function during dobutamine stress to differentiate ischemic from nonischemic cardiomyopathy and compared with wall motion score index and observed quantified stress long axis function identifies coronary artery in dilated

cardiomyopathy with greater sensitivity and specificity than standard wall motion score index, particularly in the presence of left bundle branch block. But his study group consist of unselected group of patients with dilated cardiomyopathy which included patients with prior history of myocardial infarction where the etiology of cardiomyopathy is clinically obvious and no further investigations are required for diagnosis itself.

In this context we aimed to differentiate the Ischemic from Nonischemic cardiomyopathy by using tissue doppler parameters during dobutamine stress .

REVIEW OF LITERATURE

DEFINITION OF CARDIOMYOPATHY

WHO defined Cardiomyopathies as diseases of the myocardium associated with cardiac(systolic and/or diastolic) dysfunction [41]. Cardiomyopathies constitute a group of disorders in which the dominant feature is direct involvement of the heart muscle itself. By strict definition, they are a primary myocardial disorder and not related to the effects of conditions such as pre-existing valve disease, hypertension, and coronary artery disease. From a practical standpoint, severe dysfunction due to diffuse coronary artery disease and the effects of coronary ischemia is often considered a form of cardiomyopathy (Ischemic cardiomyopathy).

CLASSIFICATION

The World Health Organisation /International Society and Federation of Cardiology Task Force recommended that cardiomyopathies be classified by the dominant pathophysiological mechanism or etiologic/pathogenic factor [41]

By mechanism	By Disorder
Dilated cardiomyopthy	Ischemic cardiomyopthy
Hypertrophic cardiomyopthy	Valvular cardiomyopathy
Restrictive cardiomyopthy	Hypertensive cardiomyopathy
Arrhythmogenic right ventricular cardiomyopthy	Inflammatory cardiomyopthy
	Metabolic cardiomyopthy
Unclassified cardiomyopthies	General system disease
	Muscular dystrophy
	Neuromuscular disorders
	Sensitive and toxic reaction
	Peripartum cardiomyopathy

DILATED CARDIOMYOPATHY

Dilated cardiomyopathy is characterized by dilatation and impaired contraction of the left or both ventricles. Both end-diastolic and end-systolic dimensions and volumes are increased, and variables of systolic function(ejection fraction, fractional shortening, systolic longitudinal motion of mitral annulus, stroke volume, and cardiac output) are uniformly decreased. With gradual dilatation more along the short axis of the left ventricle, the LV cavity becomes more spherical, with a sphericity index(long-axis dimension/short axis dimension) nearing the value of 1 (normal >1.5). Wall thickness varies but typically is within normal limits; however, the LV mass is uniformly increased. Secondary features include dilated mitral annulus and incomplete coaptation of the mitral valve leaflets responsible for the associated functional mitral regurgitation, evidence of low cardiac output, enlarged atrial cavities, right ventricular enlargement, and apical mural thrombus. Intraventricular conduction delay (left or right bundle branch block) is common and contributes further to cardiac dysfunction by causing intraventricular mechanical dyssynchrony.

It may be idiopathic, familial/genetic, viral and/or immune, alcoholic/toxic, or associated with recognized cardiovascular disease in which the degree of myocardial dysfunction is not explained by the abnormal loading conditions or the extent of ischemic damage. Histology is nonspecific. Presentation is usually with heart failure, which is often progressive. Arrhythmias, thromboembolism, and sudden death are common and may occur at any stage.

ISCHEMIC CARDIOMYOPATHY

In 1970, Burch and colleagues first used the term ischemic cardiomyopathy to describe the condition in which coronary artery disease results in severe myocardial dysfunction with clinical manifestation often

indistinguishable from those of primary dilated cardiomyopathy. Symptoms of heart failure caused by ischemic myocardial dysfunction and hibernation, diffuse fibrosis, or multiple infarctions, alone or in combination may dominate the picture of coronary artery disease. In some patients with chronic coronary artery disease, angina may be the principal clinical manifestation at one time, but later this symptom diminishes or even disappears as heart failure become more prominent. Other patients with ischemic cardiomyopathy have no history of angina or myocardial infarctions(type I silent ischemia), and it is in this subgroup that ischemic cardiomyopathy is most often confused with dilated cardiomyopathy [42].

Ischemic cardiomyopathy is the term used by some to describe the condition in which coronary artery disease causes multiple infarctions, diffuse fibrosis, or severe ischemia that leads to left ventricular dilatation with congestive heart failure and it may or may not be associated with angina pectoris. They consider ischemic dilated cardiomyopathy is usually a late result of clinically overt coronary artery disease.[43]

WHO designation of ischemic cardiomyopathy as a specific cardiomyopathy "with impaired contractile performance not explained by extent of coronary artery disease or ischemic damage" has led to confusion. If ischemia is thought not be the cause for impairment, perhaps the adjective should be replaced by one describing the perceived cause, or by idiopathic. Most clinicians use ischemic cardiomyopathy to describe dilatation and dysfunction, which they believe is caused by an ischemic insult.

The frequency with which the diagnosis of ischemic cardiomyopathy is missed should not be underestimated. In one study of 112 cardiac transplant recipients, severe coronary disease was found in all patients with a pretransplant

diagnosis of ischemic cardiomyopathy (57 percent of the total population); CAD was also present in 9 of 38(24%) patients with a pretransplant diagnosis of idiopathic dilated cardiomyopathy and in three of four with presumptive alcoholic cardiomyopathy.

Enlarged and globally hypokinetic left ventricles may at times challenge physicians concerning the etiology of this finding, since the underlying cause cannot always be determined, even after detailed history and skilled clinical evaluation, including echocardiography. Dilated cardiomyopathy, either idiopathic or secondary to specific disorders but without coronary stenoses [41], and ischaemic cardiomyopathy due to severe coronary artery disease have been used to describe left or biventricular dilatation in addition to impaired contraction. It may be difficult to distinguish between them clinically. An ischemic cause is probable in patients with a history of myocardial infarction (MI) or left ventricular (LV) aneurysm[3,4] .However, some patients with ischemic DCM have neither history nor electrocardiographic (ECG) evidence of MI[5] never complain of chest pain [6],and show diffuse, rather than regional, LV hypocontractility[3, 7]. Conversely, many patients with idiopathic DCM report frequent episodes of chest pain s and have ECG evidence of MI [9]. Ischemic cardiomyopathy is usually a late result of clinically overt coronary artery disease [45]. However, sometimes the clinical course of the disease is really occult and, indistinguishable from dilated cardiomyopathy[43,45,46]. Differentiating between this latter 'silent' ischemic and non-ischemic cardiomyopathy is imperative for both therapeutic and prognostic reasons [47,1,48]. Although ischemic cardiomyopathy bears a worse prognosis than non-ischemic cardiomyopathy [1,48,49], patients with proven hibernation may show an improved outcome after myocardial revascularization [50]. Appropriate differentiation is achieved by coronary angiography, since it still remains the gold standard. Many non-invasive techniques have been tested in this distinction

with variable accuracy [15-19, 51]. However, there are some limitations in interpretation and availability of these tests while inconsistent findings have been reported.

On reviewing the old literatures the following parameters and noninvasive techniques were used to differentiate ischemic from nonischemic dilated cardiomyopathy

1. Clinical and electrocardiographic data
2. Regional wall motion abnormalities detected at rest
3. Wall motion analysis by Dobutamine stress echocardiography
4. Right ventricular function
5. Coronary echocardiography
6. Radionuclide ventriculography
7. Electron beam computed tomography
8. Thallium-Dipyridamole scintigraphy
9. Magnetic Resonance Imaging (MRI)
10. Carotid ultrasound
11. Valvular and thoracic aortic calcification
12. Tissue doppler

CLINICAL AND ELECTROCARDIOGRAPHIC DATA

Patients with severe LV dysfunction due to coronary artery disease or nonischemic cardiomyopathy may present with identical symptoms [52]. **Chest pain** is considerd to one of the cardinal symptom of coronary artery disease. However, some patients with ischemic DCM never complaint of chest pain[9]. Conversely many patients with idiopathic DCM report frequent episodes of chest pain. ***Kannel*** and colleagues ,in 1984, analyzed the incidence and prognosis of unrecognized myocardial infarctions and found that almost half of such patients did not have chest pain and such silent infarctions were higher in women and in older men [53]. In 1973**,** ***Margolis*** and associates evaluated the incidence , prevalence, characteristics, and prognosis associated with clinically

unrecognized myocardial infarctions diagnosed by ECG changes. He observed only one third of men with unrecognized and 58% of men with recognized infarctions had history of angina pectoris ($p \leq 0.001$)[54]. In 1965, ***Massumi et al*** observed as many as 52% of patients with congestive cardiomyopathy report chest pain despite the presence of normal coronary arteries . ***Pasternac*** (1982) explained that the chest pain in idiopathic dilated cardiomyopathy is due to decreased myocardial perfusion ,both at rest and during pacing leads to subendocardial ischemia. In his study he observed three of five patients with idiopathic congestive cardiomyopathy had chest discomfort [8]**.** ***Vigna et al***, in 1996, have shown that angina was present in 53% of patients with ischemic DCM and 36% of patients with nonischemic DCM ($p= 0.994$). From these observations it is evident that patients with ischemic and nonischemic DCM can not reliably be distinguished on the basis of presence or absence of chest pain.

Ischemic cardiomyopathy may be suspected on the basis of **electrocardiographic findings**. However, the sensitivity and specificity of these data are often inadequate for individual patient management decisions and further confounded by the frequent presence of a nondiagnostic ECG with conduction abnormalities. In 1964, ***Tavel*** et al in his original article of 'abnormal Q waves simulating myocardial infarction in diffuse myocardial diseases' he demonstrated that patients with nonischemic myocardial diseases frequently had abnormal Q waves [21]. In his study 54% of patients with nonischemic DCM had pathological Q waves .On the contrary, some patients with left ventricular dysfunction due to coronary artery disease may not have ECG changes suggestive of ischemia. In 1984, of 708 myocardial infarctions among 5127 participants in the Framingham study ***Kannel et al*** had shown that 24% of patients with coronary artery disease by echocardiography did not

demonstrate any ECG changes of coronary artery disease. The sensitivity and specificity of ECG changes is further confounded by frequent presence of conduction abnormalities, especially LBBB. In Duncan's study, among 73 patients with DCM 26 patients had LBBB, 16 with ischemic DCM and 10 with nonischemic DCM. In other studies also, LBBB was present in comparable numbers in doth types of DCMs [68].

RESTING RWMA

The detection of left ventricular regional wall motion abnormalities by echocardiography or by radionuclide angiography is often thought to be a reliable indicator of the presence of significant coronary artery obstruction and prior infarction [55]**.** However, these findings have been recognized in patients with nonischemic DCM as well [43,56]. In 1984, ***Wallis et al*** [56] analyzed fifty patients with idiopathic DCM by radionuclide ventriculography and found 64% had segmental and 36% had diffuse wall motion abnormalities. ***Medina et al,*** in 1985 evaluated the usefulness of echocardiographic regional wall motion abnormalities in detecting coronary artery disease in patients with left ventricular dysfunction and a normal-sized or dilated left ventricle. 103 patients were studied by two-dimensional echocardiography and cardiac catheterization. In 60 patients (group I) who had LV Dysfunction and a dilated left ventricle by echo (patients with dilated cardiomyopathy), RWMA were detected in 44 patients and 36 (86%) of them had significant CAD, usually two- or three-vessel obstruction; of the 16 patients with dilated cardiomyopathy (DCM) and diffuse LV hypokinesis, eight (50%) had evidence of CAD. Thus the presence of RWMA by 2DE had an 83% sensitivity, a 57% specificity, and a 77% predictive accuracy in detecting CAD in patients with DCM and thus in distinguishing ischemic from idiopathic DCM. In 43 patients with LV dysfunction but normal LV size (group II), the sensitivity, specificity, and predictive accuracy of RWMA

in detecting significant CAD was 95%, l00%, and 95%, respectively. The finding, however, of diffuse LV hypokinesis does not exclude CAD in these patients, especially when the left ventricle is dilated. Though regional wall motion abnormalities had high specificity in detecting CAD in patients with severe LV dysfunction and normal LV dimensions, it had low specificity(57%) in patients with dilated left ventricle. This study has also other limitations. The assessment of wall motion abnormalities by 2DE was qualitative and subjective and may be affected by inter- or intraobserver variability. The finding of CAD in patients with DCM does not necessarily imply that CAD was the cause of congestive cardiomyopathy. A causal relationship between the two entities is not definitely established in this study**.**

Diaz and colleagues, in 1991, studied the value of two-dimensional echocardiography in differentiation of congestive and ischemic cardiomyopathy. Of 70 total patients with chronic heart failure 36 patients had nonischemic DCM and 34 had ischemic DCM. RWMAs were detected in 44% of nonischemic and 65% of patients with ischemic DCM. Diffuse wall motion abnormalities were present in 56% of patients with nonischemic DCM and 35% of patients with ischemic DCM . Regional dyssynergy in primary DCM is likely because of microcirculatory involvement and myocardial hypoperfusion [6,7]. He concluded that 2D echocardiography was not useful in patients with chronic heart failure to differentiate dilated and ischemic cardiomyopathy. From the above observations it is clearly evident that presence of RWMAs do not accurately identify patients with ischemic DCM and presence of global hypokinesia may not reliably exclude ischemic DCM

DOBUTAMINE STRESS ECHOCARDIOGRAPHY (DSE)

Echocardiography performed at rest is widely used to evaluate patients with dilated cardiomyopathy. Unfortunately, the frequency of regional wall motion abnormalities at rest in nonischemic cardiomyopathy and the presence of global dysfunction in patients with advanced ischemic cardiomyopathy prevent accurate identification of coronary artery disease [6,7]. Exercise testing is the standard noninvasive method used for detection of coronary artery disease in patients without dilated cardiomyopathy. It is not routinely used for diagnostic for diagnostic purpose in patients with dilated cardiomyopathy because of their reduced ability to perform exercise testing. Additionally, the frequency of ECG abnormalities at rest impairs interpretation of the stress ECG. Dobutamine stress echocardiography has been found to accurately identifies patients with coronary artery disease with major advantage that it is not dependant on patient's ability to exercise.

Previous studies have shown that dobutamine stress echocardiography safely and accurately identifies coronary artery disease in patients without dilated cardiomyopathy. All these studies were done in patients with normal sized ventricle. ***Sharp et al***, 1994 [15] were the first one attempted to determine the safety and accuracy of dobutamine stress echocardiography for detection of coronary artery disease in patients with dilated cardiomyopathy. He tried to determine whether stress induced changes in wall motion could distinguish patients with coronary artery disease from those without. Seventy patients with dilated cardiomyopathy underwent dobutamine stress echocardiography. Echocardiograms were obtained at baseline and at low (5 to 10 micrograms/kg body weight per min) and peak doses of dobutamine. Rest and stress left ventricular wall motion scores were derived from analysis of regional wall motion. Fifty-four subjects underwent coronary angiography. Dobutamine infusion was terminated after achievement of the

target heart rate or maximal protocol dose in 49 patients (70%), ischemia in 12 (17%), arrhythmia in 4 (6%) and side effects in 5 (7%). No patient had prolonged ischemia or sustained arrhythmia. Of those with angiographic studies, 40 had significant coronary artery disease (> or = 50% diameter stenosis). Use of the change in global wall motion score index from low to peak dose resulted in a sensitivity of 83% for dobutamine stress echocardiography and a specificity of 71% for detection of coronary artery disease. Sensitivity for detection of triple-, double- and single-vessel disease was 100%, 83% and 69%, respectively. He concluded that dobutamine stress echocardiography safely provides diagnostic information in patients with dilated cardiomyopathy. This technique has high sensitivity for multivessel coronary artery disease but only moderate specificity. In this study patients with history of MI were also included where the etiology of left ventricle dysfunction is obvious Moreover, analysis of wall motion was limited to qualitative techniques.

In 1996, ***Vigna and colleagues*** [16] studied 43 patients with left ventricular dysfunction by dobutamine stress echocardiography to distinguish between ischemic and nonischemic dilated cardiomyopathy. He selected patients less than 70 years old with DCM (LVIDd > 6.0 cm and LVEF < 40%) and without history or ECG evidence of previous MI At rest, there were more normal segments ($p < 0.001$) and a trend toward more akinetic segments (p, not significant) per ischemic than per nonischemic DCM patient. However, either at rest or with low-dose dobutamine, individual data largely overlapped. At peak dose, in ischemic DCM, regional contraction worsened in many normal or dyssynergic regions at rest (in the latter case after improvement with low-dose dobutamine); in contrast, in nonischemic DCM, further mild improvement was observed in a variable number of left ventricular areas. Thus with peak-dose dobutamine, more akinetic and less normal segments were present per ischemic than per nonischemic DCM patient (both, $p < 0.001$). A value of six or more akinetic segments was 80% sensitive and 96% specific for ischemic

DCM. His data show that analysis of regional contraction by dobutamine stress echocardiography can distinguish between ischemic and nonischemic DCM [16]. His study has some limitations. He did not perform side-by-side comparisons of wall motion on the digitized quad-screen format, so possibility of missing subtle responses to dobutamine in patients with diffuse or severe wall motion abnormalities. Moreover patients with single vessel disease frequently did not develop significant worsening of segments with peak dose dobutamine, so the sensitivity of differentiating ischemic DCM with single vessel disease and nonischemic DCM is low.

Cohen et al, in 1997 studied whether DSE is useful in differentiation of cardiomyopathy [61]. Dobutamine stress echocardiography was performed in 56 consecutive patients, mean age: sixty-two +/- twelve years. Twenty-two patients had an idiopathic dilated cardiomyopathy (group 1) and 34 had angiographically proven ischemic dilated cardiomyopathy (group 2). Wall motion score index and left ventricular ejection fraction were determined at baseline, 5 micrograms/kg/min, peak, and ten minutes after stepwise dobutamine infusion. Worsening or no change in global wall motion score was observed in 9 group 2 patients (26%) and 1 group 1 patient (5%, P = .07). No significant difference was observed with regard to wall motion score index decrease between baseline and peak dose. Left ventricular ejection fraction increase during dobutamine infusion was comparable in both groups. Thus, an ischemic response was observed more often in the coronary artery disease group, yielding a good specificity and positive predictive value although sensitivity was low. However, left ventricular function improvement did not help to discriminate patients with or without significant CAD.

Franchini [60] , in 2000, aimed to assess the values of high-dose dobutamine stress echocardiography and of Thallium-201 SPECT (exercise-reinjection-rest protocol) in differentiating between ischaemic and non-ischaemic

dilated cardiomyopathy in 37 patients with suspected myocardial ischemia, low ventricular ejection fraction (23±5%) and heart failure. Coronary artery disease was defined as >50% coronary stenosis in at least one coronary artery. By dobutamine stress echocardiography, ischaemic dilated cardiomyopathy was considered present when either an ischaemic response (biphasic response or direct deterioration) or a scar (fixed dyssynergy) was documented in atleast two segments. Twenty-three patients had ischaemic dilated cardiomyopathy, while 14 had normal coronary arteries. The presence of myocardial ischaemia and/or scar by dobutamine stress echocardiography identified patients with ischaemic dilated cardiomyopathy with a sensitivity of 100% and a specificity of 86%. Three of the four false positive results occurred in patients with left bundle branch block. He concluded that dobutamine stress echocardiography is a sensitive technique for detecting the ischaemic aetiology of dilated cardiomyopathy. However, the specificity is lower particularly when left bundle branch block is present.

THALLIUM –DIPYRIDAMOLE SCINTIGRAPHY

Thallium 201 myocardial perfusion imaging and technetium 99m human serum cardiac blood pool scanning with technetium 99m human serum albumin allow noninvasive evaluation of left ventricular myocardial perfusion and function. Thallium 201 myocardial perfusion imaging has proved useful in evaluation of coronary artery disease. Thallium 201 uptake reflects not only coronary perfusion but myocardial viability as an agent that is actively taken up and concentrated by the myocardial cell. Areas of myocardium devoid of viable muscle for whatever reason appear as "coldspots" on the thallium 201 image. Technetium 99m human serum albumin gated cardiac blood pool scanning provides a noninvasive evaluation of ventricular function. Left ventricular ejection fraction determined by this technique has correlated well with standard left ventricular contrast angiography. The combined use of these techniques had been useful in the detection and localization of

myocardial infarction. They have also been found to be useful in the evaluation of primary hypertrophic, and secondary cardiomyopathies. The purpose of the present study was to determine whether these noninvasive techniques could be used to distinguish ischemic from primary idiopathic congestive cardiomyopathy.

Bernadine and associates, in 1977 [62] evaluated radioisotope images of the heart in 13 patients with ischemic, and eight patients with idiopathic congestive cardiomyopathy, and 14 patients with normal hearts. Diagnosis was established by cardiac catheterization and/or autopsy in each of the 35 patients. The 14 normals could be readily distinguished from cardiomyopathy, and ischemic could be distinguished from idiopathic dilated cardiomyopathy in 20 of 21 patients. All patients with cardiomyopathy showed hypokinetic and dilated left ventricles, but right ventricular dilatation was evident mainly in those with idiopathic CM. TI images in the ischemic type had defects of greater than 40% of image circumference which corresponded to segmental wall motion abnormalities on gated cardiac blood pool scans(GCBPS), whereas those with the idiopathic congestive form were homogeneous or had defects of less than 20% of image circumference. Autopsy studies in 7 of 35 patients correlated TI defects of greater than 20% of circumference with transmural myocardial fibrosis.

Iskandrian et al, in 1986 examined the usefulness of resting thallium-201 myocardial scintigraphy in differentiating patients with primary cardiomyopathy from those with "ischemic" cardiomyopathy [63]. The 60 patients included in this study were those who had severe LV dysfunction with ejection fraction less than 35% as determined by radionuclide angiography, and in whom resting thallium- 201 images were available. The patients were divided into three groups: group I (n = 15) had primary cardiomyopathy based on the normal coronary angiograms or <5 % probability of CAD according to age, sex, symptoms, ECG findings, and coronary risk factors such as a history of diabetes mellitus, hypertension, abnormal lipid levels,

smoking, and a family history of premature atherosclerosis. The patients in group II (n = 20) had CAD documented by coronary angiography, which showed ~50% diameter narrowing of one or more vessels. The patients in group III (n = 25) comprised consecutive patients (21 men and four women, all between 31 and 77 years of age) with acute myocardial infarction in whom radionuclide. and thallium-201 scintigraphic studies were available -7 to 10 days after the infarction. The diagnosis of acute infarction was documented by a typical history of prolonged chest pain, appearance of abnormal Q waves, and serum enzyme changes. Resting thallium-201 myocardial scintigrams were obtained in all patients after overnight fasting, with the use of intravenous injections of 2 mCi of thallium-201. Twenty minutes after injection, thallium images were obtained in three projections (anterior, 30-degree left anterior oblique, and 65-degree left anterior oblique). Redistribution images were obtained 4 hours after injection. Most patients with primary cardiomyopathy had normal or near-normal thallium perfusion scans; thus 12 patients had either no defects, only myocardial thinning, or 13 abnormal segments. Of the 20 patients in ischemic cardiomyopathy group , 19 had more than 3 perfusion defects. The only patient with no perfusion defects on the initial scan had a diffuse abnormal washout pattern on the delayed study consistent with resting hypoperfusion. The thallium distribution pattern was different among the three groups . Extensive perfusion defects were present in only one patient in group I, whereas they were seen in 95% of patients in group II and 100% of the patients in group III. The thallium score was significantly higher (less abnormal) in group I than in the remaining two groups; only one patient in group I had a score <50, whereas 17 patients (85%) in group II and 25 patients (100%) in group III had scores ~50 (Fig. 3). The right ventricular and lung thallium uptake were not significantly different in the three groups. The limitation of this study was not all patients with primary cardiomyopathy underwent coronary arteriography; The author explained that patients who did not undergo

arteriography are unlikely candidates for CAD because of their age, sex, symptoms, and coronary risk factors.

Eichhorn and colleagues (1988) assessed the Usefulness of Dipyridamole-Thallium-201 Perfusion Scanning for Distinguishing Ischemic from Nonischemic Cardiomyopathy [17]. To determine noninvasively the etiology of left ventricular (LV) dysfunction, 22 patients with a diagnosis of cardiomyopathy determined via cardiac Cath- eterization and 5 normal control subjects underwent radionuclide ventriculography and intravenous dipyridamole-thallium-201 perfusion scanning. Both ischemically and nonischemically induced LV dysfunction had comparable global LV ejection fractions (24 +/- 6 vs 23 +/- 8%, respectively) and extent of segmental wall motion abnormalities.Right ventricular ejection fraction was significantly better in the group with an ischemic etiology of LV dysfunction (41 +/- 26 vs 13 +/- 10%, p <0.005) but significant group overlap was present. However, computer-assisted analysis of dipyridamole-thallium-201 myocardial perfusion scanning demonstrated more homogeneous myocardial perfusion in idiopathic cardiomyopathy (mean perfusion defect 25 +/- 11 vs 6+/- 6%, p <0.00l) and successfully predicted the correct etiology of LV dysfunction in 20 of 22 (91%) patients.

The basis for the difference in Tl-201 perfusion appears to reflect both differences in potential homogeneous increase of coronary blood flow and myocardial cellular metabolic activity. Coronary artery disease patients with substantial LV dysfunction frequently have occluded coronary arteries supplying the infarcted zone. Therefore, Tl-201 is unable to reach the myocardial cell for subsequent uptake. In addition, the myocardium is frequently replaced with extensive fibrous tissue metabolically unable to accumulate Tl-201. In contrast, idiopathic cardiomyopathy, although it exhibits a lower

than normal myocardial blood flow per unit mass, is still capable of increasing flow to all areas after a metabolic stress such as atria1 pacing. The lower myocardial perfusion found in dilated cardiomyopathy reflects the decreased myocardial metabolic demands resulting from the depressed functional characteristics of the cardiomyopathic ventricle. Although both ischemic and idiopathic cardiomyopathy patients exhibit decreased total coronary blood flow, the coronary artery disease patients have greater heterogeneity of regional myocardial perfusion. This is accentuated by dipyridamole and therefore results in successful delineation of these 2 entities.

Thallium-201 scintigraphy is an accepted modality in the evaluation of atherosclerotic cardiovascular disease; however, uptake is dependent on myocardial mass and cellular extraction in addition to coronary perfusion.4 Therefore, scintigraphic defects at rest may occur independently of perfusion deficits in a dilated left ventricles ***Tauberg et al,*** in 1993 [51], examined whether idiopathic dilated cardiomyopathy could be distinguished from ischemic cardiomyopathy by using parameters of defect size, severity and reversibility obtained from quantitative and qualitative assessment of exercise and redistribution thallium scans. Thallium-201 exercise testing was performed in 51 patients with coronary arteriography referred for evaluation of severe congestive heart failure. All patients had a left ventricular ejection fraction < 35%. Thirty-one ischemic patients had coronary stenosis > 70% in one or more than one artery, and 20 idiopathic patients had no coronary stenosis or identifiable cause of heart disease. Similar exercise capacity, ejection fraction and sex distribution were found in both groups. Ischemic patients more often had severe perfusion defects (97 vs 25%; p = 0.00001), large perfusion defects involving > or = 40% of the left ventricular contour (100 vs 80%; p = 0.01), and increased thallium-201 lung uptake (94 vs 65%, p = 0.01). Large severe defects were present in 90% of ischemic and only 5% of idiopathic patients. On quantitative

analysis, the area of the thallium-201 curve less than normal was greater in ischemic than idiopathic patients (14.8 +/- 9.5% vs 3.3 +/- 2.8%; p = 0.001). The degree and severity of redistribution were similar in both groups. Multivariate analysis identified the qualitative parameters of increased thallium-201 lung uptake, severe defects and large severe defects as the only independent predictors of the presence of ischemic disease. The presence of large severe defects had a 97% predictive value for ischemic cardiomyopathy. The absence of severe defects had a 94% predictive value for idiopathic dilated. This study has the limitation of retrospective data collection.

POSITRON EMISSION TOMOGRAPHY (PET)

Eisenberg JD,in 1987 had undertaken initiative to determine whether positron emission tomography (PET) performed after the intravenous injection of 11C-palmitate permits differentiation of patients with ischemic from those with nonischemic dilated cardiomyopathy. PET was performed after intravenous injection of 11C-palmitate in 10 patients with ischemic and in 10 with nonischemic dilated cardiomyopathy. Regions of homogeneously severely depressed accumulation of 11C-palmitate, representing 15% or more of the expected myocardial cross-sectional area, were observed in 8 of 10 patients with ischemic but in none of 10 patients with nonischemic cardiomyopathy. Patients with nonischemic cardiomyopathy had marked spatial heterogeneity of the accumulation of palmitate throughout the left ventricular myocardium, whereas most tomographic sections from patients with ischemic cardiomyopathy accumulated 11C-palmitate more homogeneously in regions exclusive of discrete defects indicative of remote infarction. Thus, a larger number of discrete noncontiguous regions (17 +/- 5 compared with 12 +/- 4, p less than 0.001) and greater reduction of average 11C-palmitate content (59 +/- 6 compared with 64 +/- 10% maximal myocardial radioactivity, p less than 0.05) were seen in the tomographic reconstructions from patients with nonischemic than in those from patients with ischemic cardiomyopathy. These findings support the hypothesis that

multiple myocardial infarctions underlie the process seen as dilated cardiomyopathy in patients with coronary artery disease. These findings indicate that PET permits differentiation of patients with ischemic from those with nonischemic cardiomyopathy.This study is limited by heterogenous and incompletely characterized patient groups, and discrimination between two entities was based only on the presence of discrete infarctions as made by subjective visual analysis

Mody et al, in 1991, determined if imaging of blood flow (using N-13 ammonia) and glucose metabolism (using F-18 2-deoxyglucose) with positron emission tomography can distinguish cardiomyopathy of coronary artery disease from nonischemic dilated cardiomyopathy. 21 patients with severe left ventricular dysfunction who were evaluated for cardiac transplantation were studied. The origin of left ventricular dysfunction had been previously determined by coronary angiography to be ischemic (11 patients) or nonischemic (10 patients). Images were visually analyzed by three observers on a graded scale in seven left ventricular segments and revealed fewer defects in dilated cardiomyopathy compared with ischemic cardiomyopathy for N-13 ammonia (2.7 +/- 1.6 versus 5 +/- 0.6; p less than 0.03) and F-18 deoxyglucose (2.8 +/- 2.1 versus 4.6 +/- 1.1; p less than 0.03). An index incorporating extent and severity of defects revealed more homogeneity with fewer and less severe defects in subjects with nonischemic than in those with ischemic cardiomyopathy as assessed by imaging of flow (2.8 +/- 1.8 versus 9.2 +/- 3; p less than 0.001) and metabolism (3.8 +/- 3.3 versus 8.5 +/- 3.6; p less than 0.005). Diagnostic accuracy for distinguishing the two subgroups by visual image analysis was 85%. Using previously published circumferential count profile criteria, patients with dilated cardiomyopathy had fewer ischemic segments (0.4 +/- 0.8 versus 2.5 +/- 2 per patient; p less than 0.01) and infarcted segments (0.1 +/- 0.3 versus 2.4 +/- 1.4 per patient; p less than 0.001) than did patients with cardiomyopathy of coronary

artery disease. The sensitivity for differentiating the two clinical subgroups using circumferential profile analysis was 100% and the specificity 80%. An index incorporating both number and severity of defects derived from circumferential profile analysis was significantly lower in subjects with dilated cardiomyopathy than in ischemic cardiomyopathy (0.3 +/- 0.8 versus 2.7 +/- 2.4; p less than 0.005). Thus, noninvasive positron emission tomographic imaging with N-13 ammonia and F-18 deoxyglucose is helpful in distinguishing patients with severe left ventricular dysfunction secondary to coronary artery disease from those with nonischemic cardiomyopathy, and a semiquantitative index such as circumferential profile analysis is superior to that of visual analysis alone. The main problems with PET are its nonavailability and high cost .

ELECTRON BEAM COMPUTED TOMOGRAPHY(EBCT)

Multiple studies have demonstrated a strong correlation between the presence of coronary calcium and obstructive CAD .Electron beam computed tomography (EBCT), by acquiring x-ray images of the coronary arteries, detects the presence of coronary calcium, which is invariably an indicator of intimal atherosclerosis . ***Budof et al***, in 1998, evaluated the ability of EBCT to distinguish ischemic from nonischemic causes of cardiomyopathy by evaluating heart failure patients for coronary calcification (CC). One hundred and twenty-five patients with cardiomyopathy (ejection fraction <0.40) and known coronary anatomy underwent EBCT coronary scanning to evaluate for CCs within 3 months of coronary angiography. Of the 72 patients who were found to have ischemic cardiomyopathy, 71 patients had CC by EBCT (sensitivity 99%, $p < 0.001$), mean score 798 ± 899. In comparison, among the 53 patients without significant coronary artery disease (CAD) (nonischemic cardiomyopathy), the mean score was significantly lower (17 ± 51; $p < 0.0001$), and 44 patients had a CC score of 0 (no CC present). The specificity of EBCT to exclude CAD in patients with cardiomyopathy was 83%, using a threshold

CC score of 0, and 92% for scores <80 ($p < 0.001$). Overall accuracy for determining the etiology of cardiomyopathy (differentiating ischemic from nonischemic) was 92% for this technique. In this study many many the ischemic patients had hypertension, a potential cause of nonischemic cardiomyopathy.

CAROTID ATHEROSCLEROSIS

Extracranial carotid artery disease has been strongly associated with increased prevalence of significant coronary atherosclerosis and acute coronary events, and vice versa. Furthermore, both coronary and carotid arterial trees share many risk factors that contribute to the atherosclerotic process. Ultrasonic scanning is a reliable and feasible technique to detect carotid disease. Therefore, **Androulakis et al** , in 2000,prospectively examined the value of carotid atherosclerosis in the prediction of coronary artery disease as the underlying cause of diffuse left ventricular dilatation and dysfunction in cases of undetermined aetiology [65]. In this study Seventy-eight patients with undetermined dilatation and diffuse impairment of the left ventricular contraction were studied within 28 months. They underwent carotid scan and coronary arteriography. Carotid atherosclerosis was found to be very common in ischaemic and rare in non-ischaemic cardiomyopathy. The presence of at least one abnormal carotid finding (intima–media thickness >1 mm, plaques, severe carotid stenosis) was 96% sensitive and 89% specific for ischaemic cardiomyopathy. Thus carotid scanning may be a useful screening and decision making tool in patients with cardiomyopathy of indecisive cause. Patients with carotid atherosclerosis are likely to suffer from severe coronary artery disease. Coronary angiography and subsequent myocardial viability studies, when indicated, could be considered early during their evaluation. In contrast, a negative carotid scan predicts non-ischaemic cardiomyopathy. Limitations of this study are six false–positive results of the carotid scanning were observed in individuals older than 65 years and in this age group abnormal carotid findings are more common. It is likely that the sensitivity and

specificity of carotid imaging in predicting coronary artery disease is very much dependent on age and sex. Intima–media thickness was measured in not as detailed a fashion as in most studies implicating it as a risk factor for vascular disease. Instead, the highest value at the distal common carotid artery was taken into account.

MAGNETIC RESONANCE IMAGING (MRI)

The value of cardiovascular magnetic resonance (CMR) in the treatment of heart failure is becoming established in initial functional assessment and in the determination of secondary causes. Gadolinium-enhanced CMR can also characterize areas of myocardial infarction, and limited results suggest that gadolinium enhancement is absent in nonischemic LV dysfunction. Based on these observations, ***McCrohon*** and associates , in 2003 [66] evaluated whether gadolinium enhancement might be a useful clinical tool in distinguishing LV dysfunction related to DCM or CAD and whether it may also offer new insights in DCM. Late gadolinium enhancement with CMR was performed in 90 patients with heart failure and LV systolic dysfunction (63 patients with DCM and unobstructed coronary arteries and 27 with significant CAD at angiography). We also studied 15 control subjects with no coronary risk factors and/or unobstructed coronary arteries. None (0%) of the control subjects had myocardial gadolinium enhancement; however, all patients (100%) with LV dysfunction and CAD had enhancement, which was subendocardial or transmural. In patients with DCM, there were 3 findings: no enhancement (59%); myocardial enhancement indistinguishable from the patients with CAD (13%); and patchy or longitudinal striae of midwall enhancement clearly different from the distribution in patients with CAD (28%).The author demonstrated that Gadolinium CMR is a powerful technique to distinguish DCM from LV dysfunction related to CAD . These data suggest that using the coronary angiogram as the arbiter for the presence of LV dysfunction caused by CAD could have lead to an

incorrect assignment of DCM cause in 13% of patients, possibly because of coronary recanalization after infarction.

VALVULAR AND THORACIC AORTIC CALCIFICATIONS

Cardiac valvular and thoracic aortic calcifications have previously been reported to be used as a window to diffuse atherosclerosis of the vascular system. In 2004, ***Ramazan atak*** and colleagues prospectively examined the predictive value of mitral annular calcification (MAC), aortic valve calcification(AVC), and thoracic aortic calcification (TAC) in diagnosis of coronary artery disease as the underlying cause of diffuse left ventricular dilatation and systolic dysfunction. The study included 98 consecutive patients (male/female = 76/22, mean age = 58.9 ±10.7 years, range:33 to 75 years) over the age of 30 years admitted to their clinics between October 1999 and December 2001 with signs and symptoms of congestive heart failure associated with documented cardiomegaly. Transthoracic echo cardiography and coronary angiography were performed in all patients for the evaluation of valvular calcifications and coronary status. Patients with a left ventricular end-diastolic diameter >4 cm/m2 and a left ventricular ejection fraction <45% according to the modified Simpson method were considered eligible for the study. Two-dimensional assessment of the aortic valve was done from the parasternal long and short axis and apical 4-chamber views. Aortic valve calcification was defined as bright dense echoes of >1 mm size on 1 or more cusps without restriction of leaflet motion. Criteria for MAC included an intense echoproducing structure located at the junction of the atrioventricular groove and posterior mitral valve leaflet on 2-dimensional examination. The diagnosis of TAC was assessed with the use of chest roentgenograms in which the x-ray tube was placed at the level of the seventh thoracic vertebra, at a distance of 2 meters. Calcified plaques were accepted as present when typically shaped densities were seen in the aortic arch or in the descending part of the thoracal aorta. Selective coronary angiography and left

ventriculography were performed percutaneously by Judkins technique. Luminal diameter narrowing over 50% in 1 or more epicardial coronary arteries was considered as significant coronary artery stenosis. Although there was no significant difference between the groups with and without coronary artery stenosis (CAS), with regard to presence of MAC, patients with CAS tended to have MAC more frequently (12/61, 20% vs 4/37, 11%, $p>0.05$). AVC and TAC were found to be significantly more frequent in patients with CAS compared to those without CAS (AVC, 35/61, 57% vs 4/37, 11%, $p<0.001$ and TAC, 28/61, 46% vs 2/37, 5%, $p<0.001$). While all 3 calcifications had sensitivity under 60%, and specificity and positive predictive value over 75% individually, the presence of any of them had a sensitivity of 80%, specificity of 86%, positive predictive value of 91%, and negative predictive value of 73%. Thus the presence of any of these calcifications distinguished patients with coronary artery disease with a sensitivity of 80% and specificity of 86%. The presence of aortic valvular valve and thoracic aortic calcifications seems to be associated with significant coronary arterial stenosis; however, with relatively low negative predictive values these cannot be used in clinical practice for diagnosis of underlying coronary artery disease in patients with dilatated left ventricles and impaired systolic functions.

LONG AXIS FUNCTION OF VENTRICLES

Left ventricular fibres are predominantly arranged longitudinally or obliquely in the subendocardium and subepicardium and circumferentially in the intermediate layers. The important contribution of longitudinally arranged fibres to overall ventricular function has been recognized for many years. During ventricular systole, long axis function has a major role in maintaining normal ejection fraction and associated changes in left ventricular cavity shape It has been appreciated since the time of William Harvey that normal left ventricular contraction involves the coordinated action of circumferentially and longitudinally directed fibres. During

early systole, the longitudinal and oblique fibers begin to contract first causing the long-axis to shorten, moves the mitral annulus towards the apex and the left ventricular cavity to become more spherical. After a mean delay of 25 (SD 40) ms, the circumferential fibres also begin to contract which causes transverse shortening and throughout the rest of systole both circumferential and longitudinal axes contract synchronously. Both the extent and timing of shortening and thickening of longitudinal fibers is essential to normal systolic function. Detailed observations using the superior repetition rate of M mode echocardiography demonstrate that shortening of the long axis begins during the period of isovolumic contraction. Peak long axis shortening occurs at A2 or aortic valve closure, The longitudinal fibers are distributed mainly subendocardially which makes them more vulnerable than the circumferential fibers to the effects of myocardial ischaemia. This is due to a combination of increased wall stress during systole and a limited capacity for the subendocardial arterioles to vasodilate compared with those in the intermediate and epicardial layers. Shortening and lengthening patterns of the longitudinally directed fibres are frequently abnormal in coronary artery disease. These disturbances were both systolic and diastolic in timing. In systole, there was a reduction in total long axis excursion, delayed onset of shortening with respect to the Q wave of the ECG, and reduced shortening velocity. In diastole, the onset of lengthening with respect to the second heart sound was delayed, early diastolic lengthening velocity was reduced, and relative A wave excursion was increased.

In view of the preponderance of circumferential fibres, it seems logical to deduce underlying myocardial function from the extent and velocity of their shortening; however, the picture of the underlying function reached from observing changes in left ventricular minor axis is at first sight surprising. Normal dimensions fall by 25–40% during ejection, while the normally loaded sarcomere shortens by only 10–12%.4 Furthermore, this remarkable fall in minor axis is the result of

thickening of the posterior wall to an extent much greater than would be expected from simultaneous inward movement of the epicardium . This apparent increase in myocardial mass that must underlie the observed extent of thickening can only be explained by concurrent shortening, and thus transverse thickening, of the longitudinally directed fibres. Without this longitudinal component, normal sarcomere shortening would lead to a shortening fraction of 12% and an ejection fraction of less than 30%. Thus, even normal changes in minor axis with ejection can be explained only on the basis of the combined action of the circumferential and longitudinal fibres. This suggests that the function of the latter might well be worth considering in its own right. The ventricular long axes both run from the apex to the base of the heart. The apex is clearly defined anatomically; the exact point used to locate the base has varied in different studies, but the most convenient has been the atrioventricular rings. It is possible to consider points around them separately—for example, septal and left ventricular or right ventricular free wall or to take a mean value. Long axis measurements can thus be made using any imaging method that demonstrates the ventricular cavity. Furthermore, it was demonstrated more than 60 years ago by Hamilton that the cardiac apex is fixed with respect to the chest wall.8 It follows that changes in long axis are actually measured by changes in the position of the atrioventricular rings or planes. As single structures, their position can be followed directly by M mode echocardiography and their velocity determined directly by Doppler. The long axis passes from the fibrous apex to the fibrous atrioventricular ring. Unlike with the minor axis, the extent of long axis shortening is not modified by changes in the minor axis. Measurements are thus simpler to interpret than those of the minor axis.

Long axis motion of the atrioventricular rings reflects longitudinal ventricular shortening and lengthening, and the extent and timing can conveniently be assessed with M mode echocardiography. The velocity of shortening and lengthening can be

measured using digitised M modes or tissue Doppler. Because the majority of the longitudinally arranged fibres are located in the subendocardium, long axis function therefore largely reflects subendocardial function. This is therefore useful in assessment of the consequences of ischaemia, to which the subendocardium is particularly sensitive.

Cross sectionally guided M mode echocardiograms of the left ventricular long axis can be obtained by longitudinal placement of the M mode cursor through the lateral aspect of the mitral annulus and central fibrous body, visualized on the apical four chamber view. Similarly, right ventricular long axis function can be obtained by placing the cursor through the lateral aspect of the tricuspid annulus. Motion of the apex, with respect to the transducer placed at the apex, is insignificant, thus overall lengthening and shortening of the long axis of the left or right ventricles is truly reflected by atrioventricular annular motion.

Pattern of long axis motion

The normal pattern of long axis motion is characteristic. Shortening of the long axis slightly precedes that of the minor axis, accounting for the characteristic change in cavity shape during isovolumic contraction. Peak inward motion of the long axis is synchronous with that of the minor axis and aortic closure. The proportional shortening of the long axis is, however, less than that of the short axis so that the ventricle becomes less spherical during contraction. Normal diastolic lengthening of the long axis commences promptly following mitral opening. There is little change in the long axis during diastasis, but atrial contraction pulls the ring up, with further lengthening before subsequent systolic shortening. Thus examination of longitudinal axis M mode echocardiograms can also provide useful information regarding mechanical atrial activity.6 Both mitral and tricuspid annular motion may be examined in this way. Systolic descent of the annulus

The timing and coordination of events is characteristically disturbed in coronary artery disease with delayed onset of contraction, prolonged shortening beyond aortic closure, and abnormal lengthening during early systole.These effects can be reversed by successful coronary angioplasty.The subendocardial fibres are particularly at risk in patients with dilated cardiomyopathy, both from the effects of any large or small coronary disease which may be present, but also from the indirect effects of raised left ventricular diastolic pressures In severe ventricular disease there are further characteristic abnormalities. Motion of the mitral annulus is greatly reduced or absent,7 and this has been used both in predicting prognosis,14 and as a surrogate for ejection fraction.5Typically, not only is the extent of shortening reduced, but the rates of both shortening and lengthening are as well.

TISSUE DOPPLER IMAGING (TDI)

Tissue Doppler imaging(TDI) is a novel use of ultrasound to image the motion of tissue with Doppler echocardiography. Doppler echocardiography records and displays the velocities of the moving targets . When Doppler echocardiography is used to measure the blood flow velocity , erythrocytes are targets . Their normal velocity ranges from 10 cm/sec in the venous circulation to 150 cm/sec in the arterial circulation. However, the velocities of myocardial tissue are much lower (1-20 cm/sec), but their amplitude are greater than those produced by blood. Therefore, Doppler ultrasound instruments have been modified to record the low velocities of myocardial tissue and to reject the high velocities generated by blood flow. TDI requires a high frame rate. A special function key needs to be selected to activate TDI. After TDI has been selected, the subsequent operation is identical to that used to perform regular pulsed wave Doppler echocardiography, except that TDI gain needs to be lowered from regular gain setting used for blood flow Doppler recordings and velocity scale needs to adjusted to a lower aliasing velocity (about 20-30

cm/sec or even lower) to optimize TDI signals. Also, TDI can be displayed in the color mode, just as in color imaging of blood flow. Tissue velocities are color-coded by autocorrelation: red for tissue moving towards the transducer and blue for tissue moving away from transducer. Movement and velocities of cardiac structures are regulated by the underlying systolic function and diastolic function of the heart.

The extent of systolic movement of mitral annulus correlates with LV systolic function and stroke volume. Normally, the systolic velocity (Sa or S') of annulus is more than 6 cm/sec. Early diastolic velocity (Ea or E') of the mitral annulus measured with TDI is a good indicator of LV myocardial relaxation. Longitudinal motion of mitral annulus can be appreciated visually from parasternal long-axis and apical four chamber views, but TDI records and demonstrates the velocity of longitudinal motion in numerical value. In the normal heart with normal myocardial relaxation, E' increases with exercise and dobutamine. Velocities of longitudinal mitral annulus motion are best obtained from apical views. Although various locations of the mitral annulus can be interrogated with TDI, the two most frequently used locations are septal (or medial) and lateral mitral annulus. Usually, E' from the lateral annulus is higher (normally >15 cm/sec) than the medial annulus (normally >10 cm/sec). Late diastolic velocity (Aa or A') of the mitral anulus at the time of atrial contraction increases during early diastolic dysfunction, as is the case for the mitral inflow A wave, but decreases as atrial function deteriorates. A' has been correlated with left atrial function

MITRAL ANNULUS

The mitral valve annulus is a junctional zone that separates and gives attachment to muscle of the left atrium and left ventricle and to the mitral valve

leaflets.It is not a rigid circumferential fibrous ring, but is pliable [11] and incomplete anteriorly.The annulus has two major collagenous structures, the right and left fibrous trigones. The right fibrous trigone, or central fibrous body, lies in the midline of the heart and represents the confluence of fibrous tissue from the mitral valve,tricuspid valve, membranous septum and posterior aspect of the root of the aorta The left fibrous trigone is composed of fibrous tissue at the confluence of the left margin of the aortic and mitral valves. Between the trigones ventrally, the anterior leaflet of the mitral valve is in direct fibrous continuity with the aortic root. mitral valve annulus is elliptical or nearly elliptical and changed shape during the cardiac cycle, being more circular in late diastole and flatter in systole.

LEFT VENTRICULAR LONG AXIS RESPONSE TO DOBUTAMINE

The normal left ventricular long axis response to dobutamine infusion proved to be very characteristic. Both the amplitude and peak velocity of motion increased with respect to resting values. The increase in shortening velocity with dobutamine correlated closely with that in peak aortic acceleration, long recognised as a sensitive measure of a positive inotropic stimulus, independent of loading conditions. This increase in long axis shortening velocity is thus likely to be another direct effect of the positive inotropism of dobutamine. Mitral annular systolic velocity significantly increased with only 1 mg/kg/min of dobutamine and further incremental increases occurred with each subsequent dose. A linear dose response relation was demonstrated within this narrow dosage range. A second effect of dobutamine was that systolic long axis motion started sooner after the Q wave and ended sooner after aortic valve closure, so that a consistently greater proportion of its overall shortening occurred during ejection indicating increased coordination. In individual control subjects, these altered time relations correlated with shortening of QRS duration, strongly suggesting that the resulting phase shift in long axis motion was, in part, the direct result of more rapid ventricular activation. This concurs with very early work

by *Wiggers*, who suggested that normal left ventricular contraction relies on organized activation to develop coordinate tension in both circumferential and longitudinal fibers. Overall, therefore, dobutamine had a combined effect in the normal persons, both on activation and directly on the myocardium, so that the extent and velocity of long axis shortening increased and became more synchronous with ventricular ejection.

Experimental and clinical studies have shown that during acute ischaemia, myocardial peak systolic velocity and strain rate were notably reduced or reversed within 5 seconds after coronary occlusion and were delayed. In addition, there was positive velocity after the end of ejection.6Post-systolic shortening or thickening is a sensitive marker of ischaemia and can be easily recognised by high velocity, strain rate or strain occurring during the isovolumic relaxation period, often extending into the early filling period. Accurate timing of the aortic valve closure is crucial for recognition of post-systolic shortening.However, post-systolic shortening is a normal finding in healthy subjects occurring in approximately a third of myocardial segments and, thus, is not always a marker of disease. Pathologic post-systolic shortening has high magnitude with coexisting reduction in systolic strain and strain rate, and its peak occurred later than in control subjects. Asynchronous left ventricular long axis function is common in patients with chronic stable coronary artery disease. On the left side of the heart, both the start and the end of septal long axis shortening are delayed with an ECG pattern of left bundle branch block (LBBB) (fig 1), so that both isovolumic contraction and isovolumic relaxation become uncoordinated.

LONG-AXIS FUNCTION IN DILATED CARDIOMYOPATHY

Though numerous studies are available for detection of coronary artery disease in patients with normal LV dimensions, only limited data available for differentiation of ischemic from nonischemic DCM using long axis function by tissue Doppler. The dynamics between mitral anulus motion, and, thus, motion of

the base of the heart, and filling of the left atrium and ventricle were studied by Doppler echocardiography in 12 normal subjects and 28 patients with dilated cardiomyopathy by ***Keren*** et al in 1988.During ventricular systole, the descent of the mitral anulus is towards the ventricular apex, the extent of which is 12.8 ± 1.4 mm. The end of the descent of the anulus occurs at the cessation of aortic ejection. About 100 msec later, a rapid recoil of the mitral anulus toward the atrium occurs. This rapid recoil contributes to the displacement of blood from the atria into the ventricles in early diastole. During atrial contraction, the mitral anulus moves slightly (2.4 ± 0.7 mm) toward the atrium and then returns toward its initial position within 120 msec. flow. In patients with dilated cardiomyopathy, mitral anulus motion are markedly altered in comparison with normal subjects. In all patients, motion of the mitral anulus is either reduced or absent.

Duncan and associates, in 2003 studied the differentiation of ischemic from nonischemic cardiomyopathy during dobutamine stress by left ventricular long-axis function and compared with wall motion score index. Seventy-three patients with DCM, 48 with CAD (16 with LBBB), and 25 without CAD (10 with LBBB) were studied. Long-axis M-mode, pulsed-wave tissue Doppler echograms (lateral, septal, and posterior walls), and WMSI were assessed at rest and at peak dobutamine stress. Failure to increase systolic amplitude (total amplitude minus postejection shortening) by 2 mm or early diastolic velocity by 1.1 cm/s was the best discriminator for CAD (systolic amplitude, sensitivity 85%, specificity 86%; lengthening velocity, 71% and 94%, respectively; P=NS). Both had greater predictive accuracy than did WMSI (sensitivity 67%, specificity 76%; P<0.001). The predictive accuracy of changes in septal long-axis function was similar to those of average long-axis function (systolic amplitude cutoff=1.5 mm, lengthening velocity cutoff=1.5 cm/s). However in LBBB, systolic amplitude proved to be the only significant discriminator for CAD, with sensitivity and specificity reaching 94% and 100%, respectively (P<0.01 versus early diastolic lengthening velocity).

AIM OF THE STUDY

(1) To differentiate Ischemic from Nonischemic Cardiomyopathy using Tissue Doppler Imaging- long axis function during dobutamine stress, and

(2) To compare long-axis function with wall motion score index for detecting coronary artery disease in dilated cardiomyopathy

MATERIALS AND METHODS

Setting : Department of Cardiology,
Government General Hospital,
Chennai-3.

Study Design : Single center, nonrandomized, Observational and Prospective Study.

Period of Study : From January' 2005 to December' 2006.

I. Patient selection

Patients with Dilated Cardiomyopathy who were referred to our department for the further evaluation and management were evaluated systematically by history, physical examination, electrocardiography and echocardiography along with thorough analysis of past history and risk factors for coronary artery disease.

Inclusion criteria

Patients were included in this study if they fulfilled the following inclusion criteria :

(1) Dilated cardiomyopathy with LV end-diastolic dimension > 5.6 cm and end-systolic dimension >4.0 cm.

(2) Left Ventricular ejection fraction of ≤ 40% .

(3) Patients must be in NYHA class I – III status, and

(4) Age should be ≥ 40 years.

Both male and female patients are included. Patients with both regional dyssynergy and diffuse hypokinesia are included. Patients with LBBB also included in our study.

Exclusion criteria

Patients were excluded from the study if they have any of the following.

1. Definite history or ECG evidence of prior MI
2. Patients in heart failure
3. Significant structural valvular heart diseases
4. Atrial fibrillation
5. LV aneurysm or large tissue scarring
6. Patients with congenital heart disease, prosthetic heart valves, history of myocarditis, anthracycline or other antineoplastic drug exposure, chronic renal failure
7. Uncontrolled hypertension (systolic BP>200 mmHg,diastolic BP>110 mmHg)
8. Second or third degree AV block
9. Contraindications to dobutamine infusion
10. Peripartum cardiomyopathy

Those with anterior Q waves on surface electrocardiogram or complaints of angina pectoris were included in the study in the absence of clear history of myocardial infarction.

The study cohort comprised of 32 patients with dilated cardiomyopathy of uncertain etiology, 21(65.6%) men and 11 (34.4%) women , with ages ranging from 46 to 65 years (mean 56±6) . LBBB was present in 14 (43.8%)

patients and 18(56.2%) had normal activation, i.e no LBBB. Twelve healthy persons without any symptoms and no risk factors for coronary artery disease are considered controls. Informed consent and approval of Institutional Committee were obtained.

II. STUDY DESIGN

All eligible patients underwent Tissue Doppler Imaging at rest and during peak dose dobutamine stress. LV long-axis M-mode recordings and pulsed-wave, tissue Doppler (PWTD) measurements were obtained with the cursor positioned at the septal, lateral , and posterior angles of the mitral ring. Total amplitude, systolic amplitude and postejection shortening were measured from longaxis M-mode. Both systolic and early diastolic velocities were recorded at rest and at the end of each stage of dobutamine infusion from PWTD. Measurements from the three longaxis sites were combined and average value was taken for the study. Left ventricle was divided into 16 segments, according to recommendations by American Society of Echocardiography [67]. For each segment, wall motion(systolic thickening and endocardial shortening) was qualitatively analyzed and Wall motion score index (WMSI) was calculated at rest and during peak dose dobutamine stress . Ischemia was defined as worsening of wall motion score or failure of a normal segment to develop hyperkinesis during dobutamine stress.

Coronary angiography was performed via the right femoral approach using the Judkins technique. Based on coronary angiographic finding patients were divided into two groups: Group I- Patients with ≥50% diameter stenosis in a major epicardial coronary artery or any major branch vessel constitute the ischemic DCM group,Group II - The remaining patients constitute the nonischemic DCM group. Both the groups were further divided into subgroups based on the ECG

as, having normal activation (no LBBB-subgroup A) or left bundle branch block(subgroup B).

Complete left bunble branch block

LBBB was diagnosed from ECG by the following diagnostic criteria

1. QRS duration ≥120 msec
2. Broad, notched R wave in lateral precordial leads (v 5, v 6) and usually leads I and aVL
3. Small or absent initial 'r' wave in right precordial leads (v 1,v 2) followed by deep S wave
4. Absent septal q wave in left sided leads
5. Prolonged intrinsicoid deflection (≥ 60 msec) in v 5 and v 6

Dobutamine stress echocardiography protocol

Dobutamine stress echocardiography was performed using a standard protocol[66] in all patients after obtaining informed consent. Cardiovascular drugs were stopped 48 h before the study, apart from short-acting nitrates which patients could continue until the morning of the investigation. No patient was taking a beta-receptor antagonist at the time of the study. Before the infusion was begun, a resting echocardiogram was obtained in the left lateral decubitus position using commercially available ultrasound equipment (Philips iE 33 system, 5 MHZ probe).Dobutamine stress echocardiography was performed with concurrent ECG, and blood pressure monitoring. Patients were studied in the left lateral position during continuous intravenous dobutamine infusion.

Dobutamine was infused intravenously for 3-minute stages at 5, 10, 20, 30 and 40 μg/kg/min with a maximum of 40 μg/kg/min. In patients not achieving 85% of their age-predicted maximal heart rate(defined as 220 beats . mt minus age in years for both men and women) or another end-point and without symptoms or signs of myocardial ischaemia, atropine was administered, starting with 0·25 mg intravenously and repeated up to a maximum of 1·0 mg within 4 min with a continuation of the dobutamine infusion. Throughout the dobutamine infusion heart rate and rhythm were monitored from a precordial modified lead I or II or III, and blood pressure was recorded every 3 min. Reasons for interruption of the test were: severe angina, symptomatic reduction in systolic blood pressure >40 mmHg from baseline, hypertension (blood pressure >240/120 mmHg), significant tachyarrhythmias such as atrial fibrillation or ventricular tachycardia, akinesis or dyskinesis affecting more than two segments and any serious side effect regarded as being due to dobutamine. Later side-by-side comparisons of wall motion on the digitized quad-screen format was analyzed.

LV dimensions and function

Two-dimensional echocardiography was performed from the parasternal long- and short-axis views and apical 4- and 2-chamber views. LV internal dimension at end diastole was measured at the onset of the QRS complex and systolic internal dimension was measured at the maximal excursion of the ventricular septum from a parasternal, 2-dimensional guided M-mode echocardiogram, with the cursor at the tips of the mitral valve leaflets. Left ventricular ejection fraction was calculated using modified simpson method

M-mode of mitral annulus

LV long-axis M-mode recordings were obtained with the cursor positioned at the septal, lateral , and posterior angles of the mitral ring. M-mode recordings were

obtained at a paper speed of 100 mm/s. For measuring septal and lateral mitral annular motion ,two-dimensional echo guided M-mode recordings were made from the apical four-chamber view with the cursor placed at the septal and lateral sides of the mitral annulus. (Figure 1A). Posterior mitral annulus movement is recorded from apical long axis view. The amplitude of long axis shortening (mm) was defined as the maximum excursion of the mitral annulus during systole. Total amplitude(TA) was defined as maximum displacement of the ring between the onset of QRS and peak inward movement at or after end of systole. Postejection shortening (PES) was measured as the amplitude of shortening after the systole. Systolic amplitude(SA), representing long-axis displacement during ventricular ejection, was calculated by subtracting PES from total amplitude(Figure 1B).

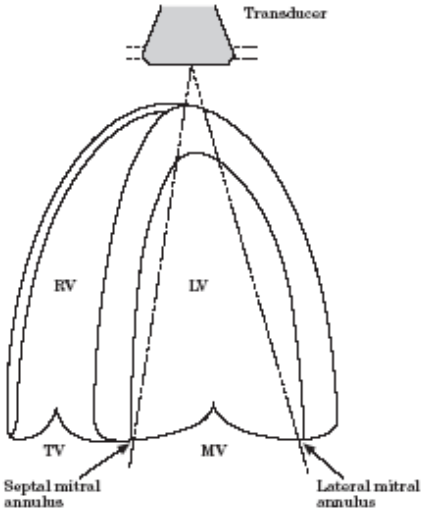


Figure.1A - M-mode cursor placement for measurement of mitral annular motion from apical four chamber view. The M-mode cursor is placed first at the septal and then at the lateral side of the mitral annulus

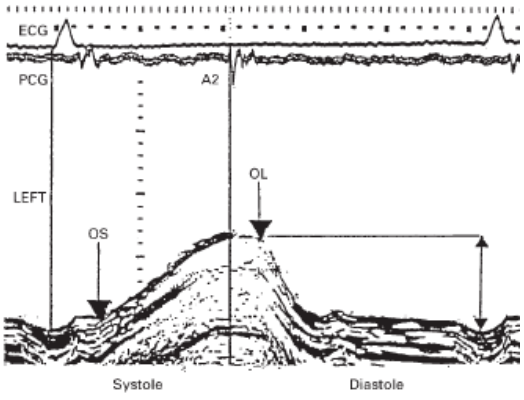
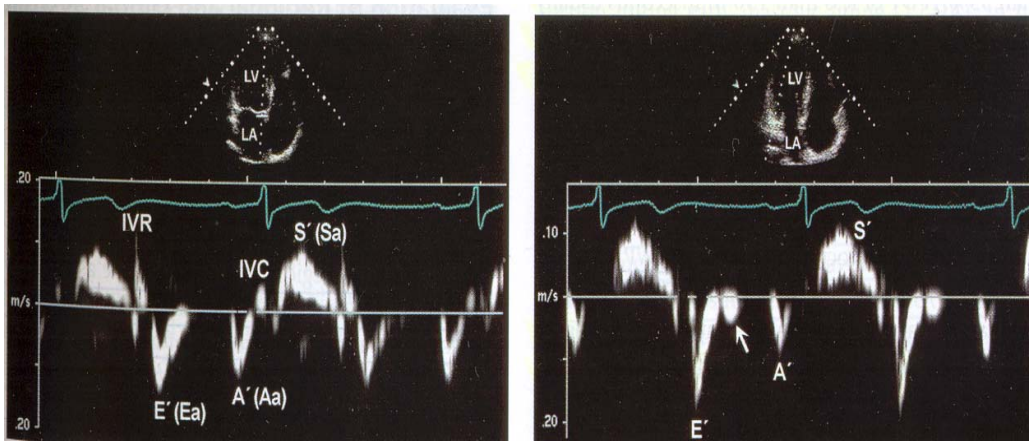


Figure.1B - An example of M mode recording of the left sided long axis along with an electrocardiogram and phonocardiogram. First vertical line represents the onset of the Q wave and the second represents the first high frequency component of the aortic component of the second heart sound. OS, onset of shortening; OL, onset of lengthening; A2, aortic component of the second heart sound; ECG, electrocardiogram; PCG, phonocardiogram

Parameters are measured at rest and end of each stage of dobutamine stress. Measurements from the three longaxis sites were combined and average value was taken for the study.

Pulsed-wave tissue Doppler of LV long axis

LV long-axis, pulsed-wave, tissue Doppler (PWTD) measurements were obtained with the cursor positioned at the lateral, septal, and posterior angles of the mitral ring.(Figure 2). A Doppler velocity range of 30 cm/s was selected to display systolic and early diastolic velocities. Both systolic and early diastolic velocities were recorded at rest and at the end of each stage of dobutamine infusion .All PWTD recordings were obtained at a paper speed of 100 mm/s. To make data comparable with previous studies of wall-motion score index (WMSI), measurements from the 3 longaxis sites were combined for PWTD Because LBBB is frequently associated with asynchronous septal contraction, septal long-axis values are also presented separately.



A **B**

Figure. 2 – Tissue Doppler imaging of the septal (A) and lateral mitral annulus in a normal Subject. In tissue Doppler imaging of the annulus , there are three major velocities: Systolic velocity (S' or Sa) ,early diastolic velocity (E' or Ea) and late diastolic velocity (A'or Aa).IVC-Isovolumic contraction. IVR-Isovolumic relaxation

Wall Motion Score Index

Two dimensional echocardiography was performed from the parasternal long- and short-axis views and from apical four- and two-chamber views. A full sequence of images was recorded at the end of each 3 min stage. Baseline and peak images were analysed using the 16-segment model of the left ventricle as recommended by the American Society of Echocardiography and WMSI (summation of all segments scored divided by the number of segments scored) was calculated[67]. Segmental wall motion was graded 1 to 4 (where 1=normal wall motion at rest and hyperkinesis with stress, 2=hypokinesis at rest or segments with normal amplitude at rest but a reduction with dobutamine, 3=akinesis, and 4=dyskinesis).Ischemia was defined as worsening of wall motion score or failure of a normal segment to develop hyperkinesis during dobutamine stress. Multivessel involvement was defined as a new wall motion abnormality in an arterial site distant from the resting wall motion abnormality.

III. CORONARY ANGIOGRAM

Coronary angiography was carried out via the right femoral approach using the Judkins technique and standard projections. Significant CAD was defined as ≥50% reduction in the absolute lumen diameter of a major epicardial artery or major branch vessel(e.g. first diagonal of LAD or obtuse marginal of Cx) estimated by eye. The results were interpreted by observers blinded to the results of stress echocardiography

IV. STATISTICAL ANALYSIS.

Differences between groups are reported as mean±SD. Rest and stress values within each study group were compared with a paired Student's t test. An unpaired Student's t test was used to compare values between groups. In view of multiple t tests, a significant difference was set at $P<0.01$. The incremental value of measurements of long-axis function and WMSI were tested with a stepwise logistic regression, and a receiver operating characteristic curve was constructed to establish the sensitivity and specificity of a range of threshold changes in long-axis and WMSI values for angiographic CAD.

RESULTS

Clinical data

A total of thirty two cases were included in this study. Among this, 21(65.6%) were males and 11 (34.4%) were females , with ages ranging from 46 to 65 years (mean 56±6) . Most of the patients were in NYHA class II or III. LBBB was present in 14 (43.8%) patients and 18(56.2%) had normal activation, i.e no LBBB. Patients were divided into two groups based on presence or absence of significant coronary artery disease on coronary angiography: Group I- Nonischemic cardiomyopathy (no siginificant CAD), Group II- Ischemic cardiomyopathy (significant CAD +) Baseline characteristics of the study group is shown in table.1.

Table 1. Baseline characteristics of the study population

		Nonischemic Cardiomyopathy		Ischemic Cardiomyopathy		
	Controls	NO LBBB	LBBB	NO LBBB	LBBB	
Variable	(n=12)	(n=10)	(n=8)	(n=8)	(n=6)	p value
Mean age(±SD)yrs	54±9.1	56±4.4	58±5.2	59±8.0	60±4.4	
(Range)	(40-62)	(42-55)	(45-66)	(48-65)	(43-68)	0.201
Gender(M/F)	8/4	6/4	6/2	5/3	4/2	
Male %	66	60	75	62.5	66.6	0.022
NYHA II n (%)	-	6 (60%)	5 (62.5%)	5 (62.5%)	4(66.7%)	0.842
NYHA III n (%)	-	4 (40%)	3 (37.5%)	3 (37.5%)	2(33.3%)	0.645
Angina n (%)	-	4(40)	3(37.5)	5(62.5)	2(33.3)	0.994
SBP mmHg	130±14	134±10	132±11	128±12	124±10	0.840
DBP mmHg	76±11	82±8	80±6	78±12	76±8	0.523
Smoking %	-	6(60)	4(50)	5(62.5)	4(66.6)	0.416
Diabetes %	-	5(50)	3(37.5)	4(50)	2(33.3)	0.014
Hypertension	-	4(40)	4(50)	6(75)	3(50)	0.510
EDD mm	48±4	70±6	66 ±8	72±6	70±5	0.994
ESD mm	34±6	58±5	57±4	60±6	59±8	0.073
LVEF %	60±4	31±9	30±11	33±8	28±6	0.842

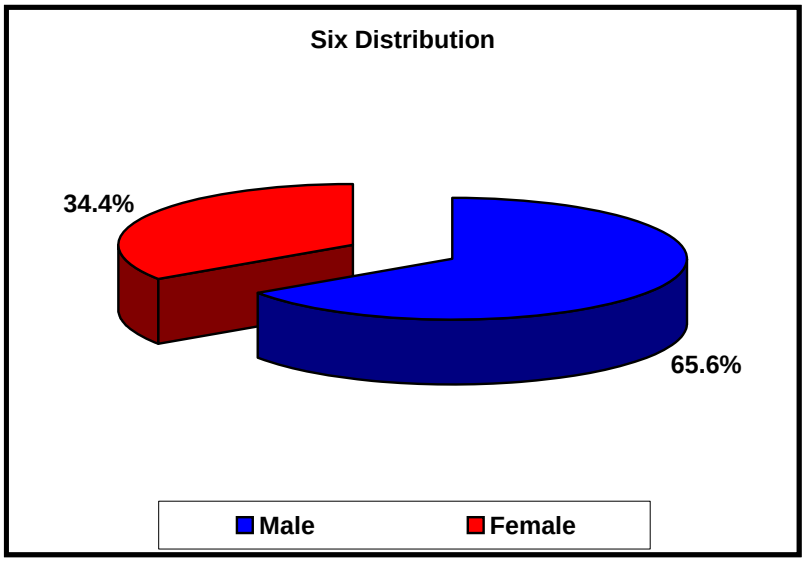


Fig. 3

Each group is further divided into subgroups based on normal activation or presence of LBBB in electrocardiography

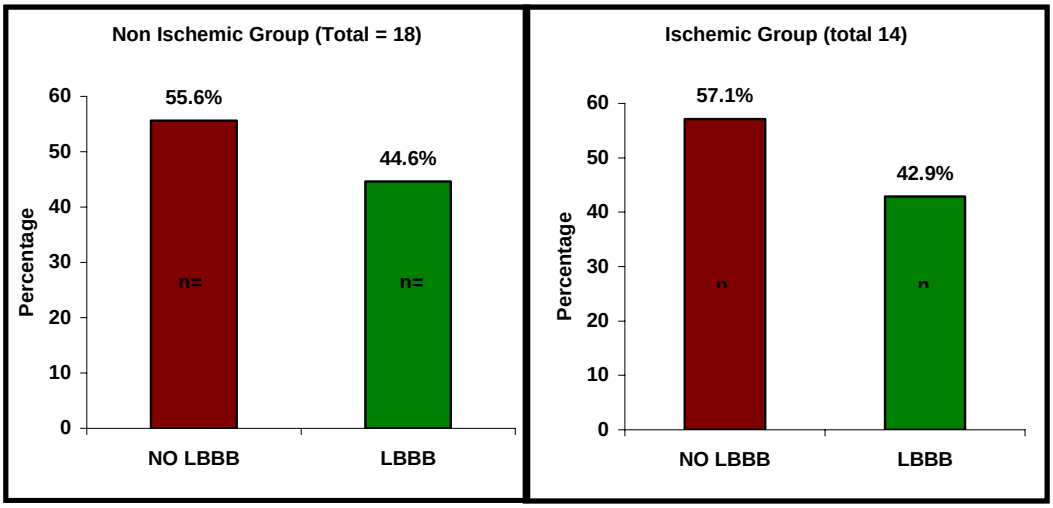


Fig. 4

Chest pain was present in seven patients in group I (4-normal activation, 3- LBBB) and in seven patients in group II (5-normal activation, 2-LBBB). In both the groups chest pain was more common in patients with normal activation , though it is not significant (table 1 & 2).

Table 2 Prevalence of Chest pain

Group	Normal Activation	LBBB
I (n = 18)	4 (40%)	3 (37.5%)
II (n=14)	5 (62.5%)	2 (33.3%)

Patients in both the groups had LV end-diastolic dimension of more than 6 cm. Patients with both CAD and LBBB had significantly greater LV end-diastolic and end-systolic dimensions (Table 1) than did patients with either alone (all $P<0.01$). LV dysfunction was equally severe in both ischemic and nonischemic DCM groups.

Coronary angiography findings

Fourteen patients had significant coronary artery disease which constitute ischemic cardiomyopathy group (group I).The extent of CAD was not different in

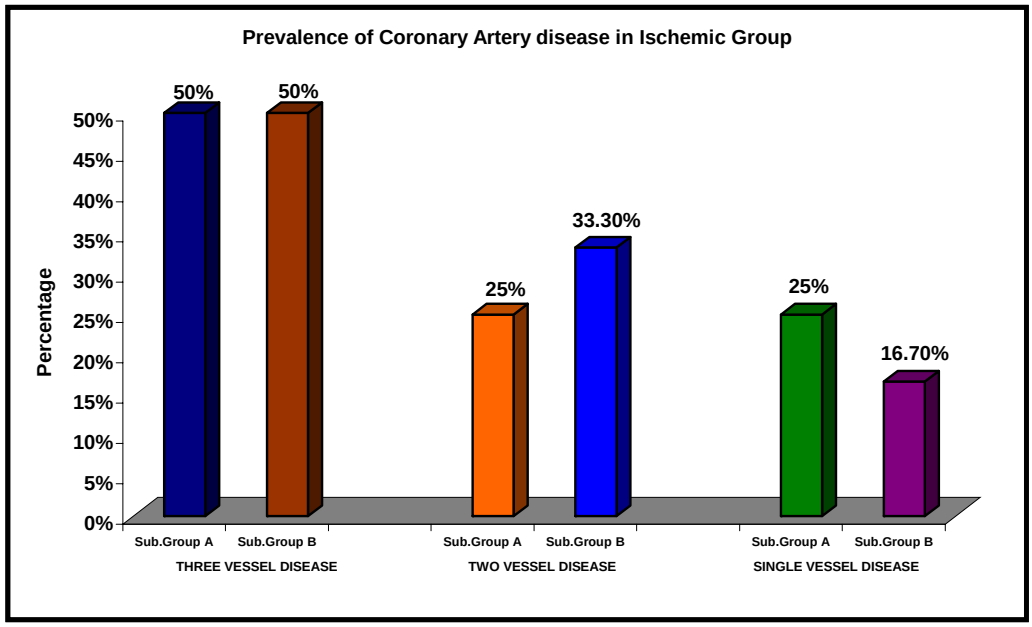


Fig. 5

subgroups of ischemic cardiomyopathy group, although two vessel disease was commoner in patients with LBBB (Fig 6A & 6B). In this group 7 patients had three vessel disease and 4 in group A, 3- group B ,most of them had severe involvement of LAD. Two vessel disease was present in four patients-2 in each group(2-LAD+RCA,1-LAD+LCX and 1-RCA+LCX). Three patients had single vessel disease-all LAD involvement(2- group A, 1-group B) (Table 1).

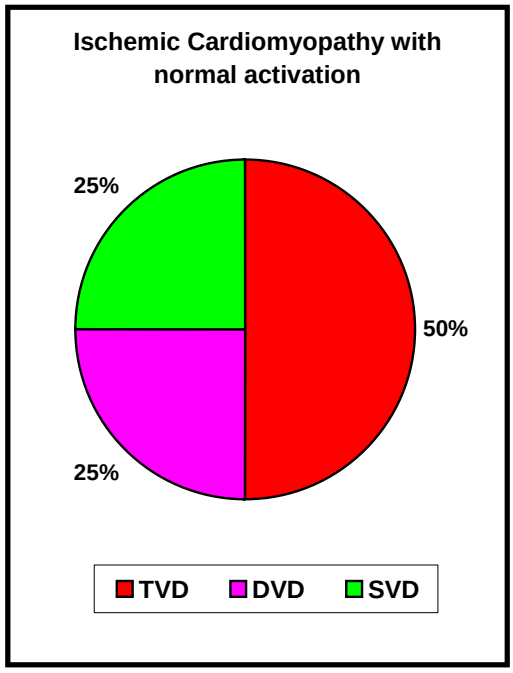


Fig.6A

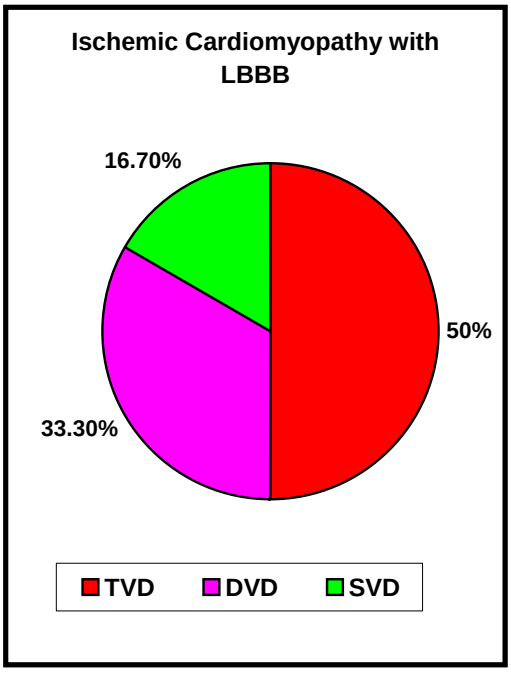


Fig. 6B

In nonischemic cardiomyopathy group, 12 patients had normal coronary anatomy and 6 had insignificant lesions of less than 50% luminal diameter.

Dobutamine stress end-point

No differences in mean infused dose of dobutamine, achievement of maximal dose of dobutamine and of 85% of maximal predicted heart rate. Also no difference was seen in the peak dose dobutamine and blood pressure. Eight

Table 3. Clinical details of study population

Variable	Controls (n=12)	Nonischemic Cardiomyopathy No LBBB (n=10)	Nonischemic Cardiomyopathy LBBB (n=8)	Ischemic Cardiomyopathy No LBBB (n=8)	Ischemic Cardiomyopathy LBBB (n=6)
EDD mm	48±4	64±6	66 ±6	66±8	70±5*†
ESD mm	34±6	57±5	57±4	60±6	62±8*†
Three vessel disease	0	0	0	4	3
Two vessel disease	0	0	0	2	2
Single vessel disease	0	0	0	2	1
Stress echo endpoint					
Dobutamine dose, (mcg/kg/mt)	30±5	30±5	35±5	30±5	35±5
Peak HR /mt	122±10	116±18	110±14	121±11	120±16
Chest pain,n	0	1	1	3	2
Breathlessness,n	0	0	1	2	2
Ventricular ectopics	0	2	2	2	1
Hypotension	0	0	1	0	2
VT	0	0	0	0	0

Values are mean±SD. NA indicates normal activation; EDD, end-diastolic dimension; and ESD, end-systolic dimension.*P<0.001, ischemic cardiomyopathy (LBBB) vs nonischemic cardiomyopathy (LBBB).†P<0.01, ischemic cardiomyopathy: LBBB vs NA.

patients required atropine for achieving target heart rate (five in group II and three in group I).5 patients with ischemic cardiomyopathy developed chest pain during stress, but only in two patients in nonischemic group. None of the patients had VT in either group.(Table 3). Hypotension developed in three patients (one in group I, two in group II).

Changes in Average Long-Axis Function With Stress

Table 4. Changes in Average Long Axis Function With Stress

Variable	Controls (n=12)	Nonischemic Cardiomyopathy No LBBB (n=10)	Nonischemic Cardiomyopathy LBBB (n=8)	Ischemic Cardiomyopathy No LBBB (n=8)	Ischemic Cardiomyopathy LBBB (n=6)
Rest					
TA, mm	12.4±1.3	10.8±1.8 *	7.2±1.2 ††	8.8±2.4 ‡‡	6.0±1.6 §
SA, mm	12.4±1.3	10.8±1.8 *	6.3±0.9 ††	7.8±1.9 ‡‡	5.3±1.8 § §
PES, mm	0±0	0±0	1.0±0.7 ††	0.6±0.5 ‡‡	1.0±0.6
SV, cm/sec	7.6±1.6	3.6±1.5 * *	3.4±1.2	3.9±1.3	2.4±1.2 §
EDV, cm/sec	7.2±1.8	5.2±1.0 *	5.0±1.4	3.9±1.2 ‡‡	2.4±1.0 §
WMSI	-	2.4±0.18	2.08±0.36†	2.2±0.22 ‡‡	2.36±0.2 §
Response to stress					
Δ TA, mm	+3.8±0.7¶¶	+2.9±1.5 ¶¶	+2.0±0.9 ¶¶	+1.4±0.9 ¶¶	+1.3±1.1 ¶¶
Δ SA, mm	+3.8±0.7 ¶¶	+2.9±1.5 ¶¶	+2.8±1.0 ¶¶	+0.6±1.2	0.5±1.5
Δ PES, mm	0±0	0±0	−0.9±0.6 ¶	+0.8±0.6 ¶¶	+0.8±0.8 ¶¶
Δ SV, cm/s	+4.2±1.6 ¶¶	+3.6±2.2 ¶¶	+3.6±2.3 ¶¶	+1.2±0.8 ¶¶	+1.1±1.0 ¶
Δ EDV, cm/s	+2.4±0.9 ¶¶	+4.5±2.1 ¶¶	+2.9±1.9 ¶¶	+0.5±1.6	+0.2±1.8
WMSI	-	-0.36±0.26 ¶¶	+0.06±0.28	+0.07±0.28	+0.05±0.25

Values are mean±SD. NA indicates normal activation; TA, total amplitude; SA, systolic amplitude; SV, systolic velocity; and EDV, early diastolic velocity. *P<0.01, **P<0.001, nonischemic cardiomyopathy (NA) vs controls at rest. †P<0.01, ††P<0.001, nonischemic cardiomyopathy: LBBB vs NA at rest. ‡P<0.01, ‡‡P<0.001, ischemic cardiomyopathy (NA) vs nonischemic cardiomyopathy (NA) at rest. §P_0.01, §§P_0.001, ischemic cardiomyopathy (LBBB) vs ischemic cardiomyopathy (NA) at rest. ¶P<0.01, ¶¶P<0.001, stress vs rest within group.

In nonischemic cardiomyopathy (Table 4), the average longaxis response to stress was similar to that of control subjects, irrespective of LBBB. Total amplitude, systolic amplitude, systolic velocity, and early diastolic velocity all increased (all P<0.001) during peak dose dobutamine; PES did not appear in any patient; and in those with LBBB, PES amplitude fell (P<0.01).

In ischemic cardiomyopathy (Table 5), systolic amplitude and early diastolic velocity failed to increase, and PES was exaggerated (P<0.001) in patients with normal activation. Systolic velocity did increase, but by less than in nonischemic cardiomyopathy (P<0.01). With LBBB, systolic amplitude, systolic velocity, and early diastolic velocity increased even less with stress, whereas PES was greater (all P<0.01).

Changes in Septal Long-Axis Function With Stress

In nonischemic cardiomyopathy group,the septal long-axis response to stress

Table. 5. Septal Long-axis Function

		Nonischemic Cardiomyopathy		Ischemic Cardiomyopathy	
Variable	Controls (n=12)	No LBBB (n=10)	LBBB (n=8)	No LBBB (n=8)	LBBB (n=6)
Rest					
TA, mm	13.0±2.1	11.3±2.8	6.4±1.5†	7.3±2.9‡‡	4.6±2.2§
SA, mm	13.0±2.1	11.3±2.8	4.4±1.6†	6.4±2.7‡‡	3.4±2.4§
PES, mm	0±0	0±0	1.7±0.9†	1.0±1.1‡	1.2±1.2
SV, cm/sec	6.8±1.5	3.4±1.0*	3.4±0.9	2.7±0.6	1.1±1.3§
EDV, cm/sec	5.6±1.4	5.2±1.8	4.6±2.0	3.3±1.6‡‡	0.8±1.7§
Response to stress					
Δ TA, mm	+3.6±2.4¶¶	+3.2±1.2¶¶	+1.2±0.5¶¶	+1.0±1.6¶	+1.3±1.5¶
Δ SA, mm	+3.4±2.3¶¶	+3.2±1.0¶¶	+2.6±0.9¶¶	-0.4±1.7	+0.4±0.1
Δ PES, mm	0±0	0±0	−1.4±1.0¶¶	+1.3±1.2¶¶	+0.9±1.2¶
Δ SV, cm/s	+4.2±1.8¶¶	+3.6±1.6¶¶	+3.1±2.2¶	+1.7±1.9¶	+1.4±1.6
Δ EDV, cm/s	+2.7±1.67¶¶	+3.8±1.9¶¶	+2.4_1.7 ¶	+1.3±1.5¶	+0.5±2.4

Values are mean± SD. NA indicates normal activation; TA, total amplitude; SA, systolic amplitude; SV, systolic velocity; and EDV, early diastolic velocity. *P<0.001, nonischemic cardiomyopathy (NA) vs controls at rest. †P<0.001, nonischemic cardiomyopathy: LBBB vs NA at rest. ‡P_0.01, ‡‡P_0.001, ischemic cardiomyopathy (NA) vs nonischemic cardiomyopathy (NA) at rest..§P<0.00l, ischemic cardiomyopathy (LBBB) vs ischemic cardiomyopathy (NA) at rest. ¶P<0.01, ¶¶P<0.001, stress vs rest within group.

was similar to that in control subjects in patients with LBBB (Table 4),. By contrast, septal systolic amplitude and velocities failed to change in ischemic cardiomyopathy and LBBB (Table 5), but PES amplitude was increased (P<0.01).

Dobutamine stress echocardiography and Wall Motion Score Index (WMSI)

At rest **:** Global LV function was severely depressed in both ischemic (ejection fraction, 0.31±0.9 and 0.30±11; WMSI, 2.4±0.18 and 2.08±0.36 in subgroup A and B respectively, p=NS) and nonischemic groups (ejection fraction, 0.33±0.8 and 0.28±0.6; WMSI, 2.2±0.22 and 2.36±0.2 in subgroup A and B respectively, p=NS). There was a trend toward more akinetic segments per patient with ischemic DCM than per patient with nonischemic segment (p=NS). Although LV hypocontractility tended to be more homogenously distributed in patients with nonischemic DCM, large overlaps of individual data were observed at baseline between the two groups. In both the groups higher WMSI was found to be correlated with presence of three vessel disease.

Low dose dobutamine **:** At low dose dobutamine, contractility improved and WMSI decreased in both groups. With respect to baseline, there was an increase in normal segments and a decrease in akinetic segments, either per ischemic or nonischemic DCM patient. However, with respect to baseline, significant decrease in severely hypokinetic segments per patient is seen only in nonischemic DCM group.

Peak dose dobutamine **:** Global WMSI fell further with stress in nonischemic cardiomyopathy and normal activation (group IA), i.e significant of number of segments showed improved contractility with PD dobutamine ($P<0.001$). But WMSI increased in all other group, particularly so in patients with ischemic cardiomyopathy and normal activation. Biphasic response was noted in 11 of 14 patients with ischemic cardiomyopathy and 2 of 18 patients with nonischemic cardiomyopathy. The higher increase in WMSI in ischemic group is found in patients with extensive involvement of coronary arteries (three and two vessel disease) .

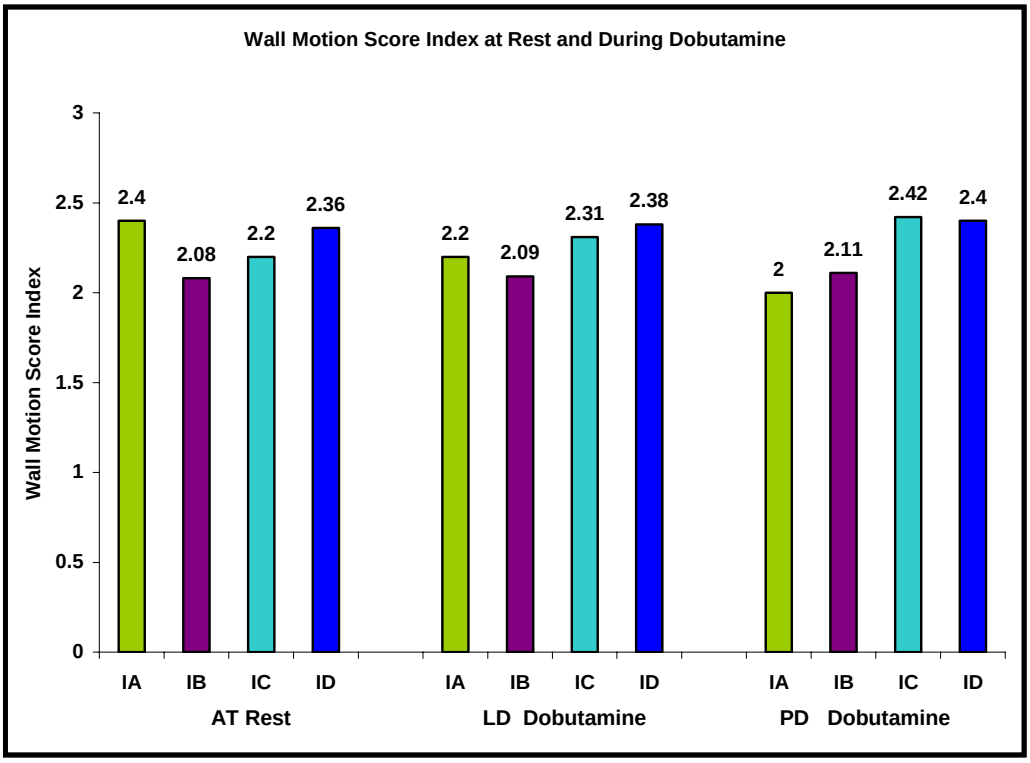


Fig.7

With respect to baseline, the number of segments showing improved contractility was increased in both groups during low dose dobutamine. During peak dose dobutamine further increase in contractility was noted only in nonischemic group but decreased in ischemic group i.e. biphasic response (Figure 7).

Prediction of CAD From Changes in Average Long-Axis and WMSI Values With Stress

Stress-induced changes in average long-axis amplitude, shortening, and early diastolic lengthening velocities and in WMSI were all univariate predictors of CAD

Table 6. Predictors of CAD

Variable	*t*	AUC (CI)	Cutoff	X^2	*P*	Sensitivity, %	Specificity,%
Δ Average SA, mm	+4.0	0.90 (0.84–0.96)	+1.96	16.6	<0.001	86	90
Δ Average SV, cm/s	+3.4	0.76 (0.65–0.90)*	+2.67	11.4	<0.001	90	70
Δ Average EDV, cm/s	+3.3	0.85 (0.70–0.92)	+1.04	10.0	<0.001	78	94
Δ Average TA, mm	2.8	0.66 (0.60–0.82)**	+2.0	8.8	0.003	70	60
Δ WMSI	-2.5	0.66 (0.58–0.80)**	-0.13	6.8	0.006	62	88
Septal predictors of CAD							
All patients (n=36)							
Δ Septal SA, mm	+3.6	0.90 (0.81–0.96)	+1.3	14.8	<0.001	89	100
Δ Septal SV, cm/s	+2.6	0.72 (0.57–0.85)†	+1.8	7.9	<0.01	75	76
Δ Septal EDV, cm/s	+2.6	0.80 (0.66–0.88)	+1.5	8.0	<0.01	71	94
Δ Septal TA, mm	+3.1	0.74 (0.62–0.83)†	+0	9.6	<0.01	40	98
LBBB (n=14)							
Δ Septal SA, mm	+2.1	0.89 (0.82–0.96)	+1.3	6.0	<0.01	94	100
Δ Septal SV, cm/s	+1.8	0.64 (0.40–0.87)‡	+1.8	2.6	NS	76	68
Δ Septal EDV, cm/s	+1.5	0.73 (0.50–0.82)‡	+1.5	2.0	NS	67	78
Δ Septal TA, mm	+0.6	0.60 (0.40–0.80)‡	+0	0.6	NS	42	97

t indicates coefficient/SE; AUC, area under curve; CI, 95% confidence interval; SA, systolic amplitude; SV, systolic velocity; EDV, early diastolic velocity; and TA, total amplitude. *P<0.01, **P<0.001, vs AUC for average SA. †P<0.01, vs AUC for septal SA (all patients).‡P<0.01, vs AUC for septal SA (LBBB alone).

(Table 6). The best discriminators, however, were changes in systolic amplitude and early diastolic lengthening velocity (both P<0.001). An increment of 2 mm in systolic amplitude correctly identified 12 of 14 patients with CAD and 16 of 18 patients without CAD (sensitivity 86%, specificity 89%), whereas an increment of 1.0 cm/s in early diastolic lengthening velocity identified 11of 14 patients with CAD and 17 of 18 patients without CAD (sensitivity 78%, specificity 94%). The predictive accuracy of both systolic amplitude and early diastolic velocity for detecting CAD was significantly greater than that of changes in WMSI (P<0.001). In the LBBB group, the same cutoff criteria gave a sensitivity and specificity of 88% and 89% (systolic amplitude), 70% and 88% (early diastolic lengthening velocity; difference NS), and 62% and 88% for WMSI (P<0.001 versus systolic amplitude), respectively.

Prediction of CAD From Septal Long-Axis Values

Changes in septal systolic amplitude in the study population had a predictive accuracy similar to that of average long-axis function, with systolic amplitude (cutoff=1.5 mm) and early diastolic lengthening velocity (cutoff=1.5 cm/s) being the best discriminators (Table 5). However, in the LBBB group, systolic amplitude proved to be the only significant discriminator for CAD (cutoff=1.5 mm), with sensitivity and specificity reaching 94% and 100%, respectively ($P<0.01$ versus early diastolic lengthening velocity).

DISCUSSION

The underlying diagnosis in patients presenting with left ventricular dilatation and impaired systolic function, and no evidence of a known cardiac or systemic disease, sometimes remains clinically undetermined. Individuals who never experienced angina or myocardial infarction may have unrecognized extensive coronary artery obstruction, whereas patients with angina may lack coronary stenoses [46]. Accurate distinction of ischaemic from non-ischaemic cardiomyopathy is fundamentally achieved by coronary angiography, which also delineates the coronary anatomy before considered revascularization. Several techniques have been utilized for non-invasive differentiation. Up to 60% of patients with severe cardiomyopathy have left bundle branch block (LBBB) , which can mask the evidence of previous infarction and make the interpretation of electrocardiographic changes with exercise testing (without imaging) impossible [7] Radioisotope perfusion imaging and stress echocardiography have been acceptable and feasible methods [15-17,51]. However, overlaps and dissimilar findings have been described especially in low ejection fractions and severe wall motion abnormalities. Positron emission tomography is extremely useful in assessing myocardial viability and also precisely differentiates between ischaemic and dilated cardiomyopathy [19]. However, it is problematic in diabetic patients and its application is limited because of unavailability and high cost. Longitudinal myocardial fibers are predominately subendocardial and are sensitive to ischemia and abnormal activation. Furthermore, stress-induced changes in long-axis function can be measured objectively. Comparing long-axis behavior at rest and during stress in ischemic and nonischemic cardiomyopathy provide define criteria for differentiating between them.

Stress-Induced Changes in long axis function

The normal left ventricular long axis response to dobutamine infusion proved to be very characteristic. Both the amplitude and peak velocity of motion increased with respect to resting values. Hoglund et al. in 1988, first documented changes in the left ventricular long axis during systole in healthy volunteers and suggested these could be used to assess ventricular function in man. Simonson and Schiller [39] showed that a reduction in long axis function, called descent of the base in their study, correlated well with impaired left ventricular ejection fraction in a large group of patients including those with coronary artery disease. Only limited data is available regarding use of long axis function in differentiation of cardiomyopathies. Mishra et al [38] in 2002 compared long-axis function and wall motion analysis for the detection of significant coronary artery stenoses in patients with single and multivessel disease. A blunted increase in mean long-axis shortening of < 2.5 mm was the best discriminator for coronary artery disease (sensitivity 85%, specificity 81%). Using this threshold, long axis function had a sensitivity of 88% and specificity 89% for the detection of coronary artery disease in patients with normal resting wall motion while wall motion abnormality analysis had a sensitivity 73% and specificity 94%. But most of the patients in his study had normal LV dimensions.

Duncan et al, in 2003 first used long axis parameters to differentiate ischemic and nonischemic cardiomyopathy [45]. He suggested failure to increase systolic amplitude by 2 mm or early diastolic velocity by 1.1 cm/s was the best discriminator for CAD (systolic amplitude, sensitivity 85%, specificity 86%; lengthening velocity, 71% and 94%, respectively; P=NS). It had greater predictive accuracy than did WMSI (sensitivity 67%, specificity 76%; P<0.001). The predictive accuracy of changes in septal long-axis function was similar to those of average long-axis function (systolic amplitude cutoff =1.5 mm, lengthening velocity cutoff =1.5 cm/s). However in LBBB, systolic amplitude proved to be the only significant

discriminator for CAD, with sensitivity and specificity reaching 94% and 100%, respectively (P<0.01 versus early diastolic lengthening velocity).

In our study Stress-induced changes in total long-axis amplitude, systolic long-axis velocities, and WMSI all distinguished ischemic from nonischemic cardiomyopathy

Average systolic and total amplitude, and lengthening velocities

In our study average systolic amplitude cut-off of 1.96 mm(2 mm) differentiated ischemic and nonischemic cardiomyopathy with sensitivity of 86% and specificity of 90% which comparable with Duncan's study. Failure to increase average total amplitude of 2.0 mm had lower sensitivity and specificity (70% and 60% respectively).Average end-diastolic velocity had less sensitivity and more specificity than average systolic velocity. Blunted increase in EDV (cut off=1.04) had sensitivity of 78% and specificity of 94%.

Septal predictors of coronary artery disease

Because LBBB is frequently associated with asynchronous septal contraction, septal long-axis values are also presented separately. In patients with normal activation sepatal systolic amplitude, total amplitude, end-diastolic and systolic velocities all distinguished ischemic from nonischemic cardiomyopathy. But in patients with LBBB, failure to increase septal systolic amplitude by <1.3 mm with stress was the only discriminator for CAD and was highly sensitive and specific (94% sensitivity and 100% specific). This is also comparable with Duncan's observation, but cut-off value in his study is higher (1.5 mm). This may be partially explained by the relatively more severe LV dysfunction in our patients.

On summary, though Stress-induced changes in total long-axis amplitude, systolic long-axis velocities, and WMSI all distinguished ischemic from nonischemic cardiomyopathy,the best overall predictors of CAD, however, were changes in long-axis systolic amplitude and early diastolic lengthening velocity. Failure to increase systolic amplitude by 2 mm or early diastolic lengthening velocity by 1.0 cm/s with stress, even when LBBB was present, had a greater predictive accuracy than did changes in WMSI. In LBBB, failure to increase septal systolic amplitude by >1.3 mm with stress was the only discriminator for CAD and was highly sensitive and specific.

Wall motion score index

The sensitivity of WMSI in previous studies for detecting CAD in dilated cardiomyopathy ranged between 26% and 100%. In Mishra's observation wall motion abnormality analysis had a sensitivity 73% and specificity 94% [38]. Sharp et al demonstrated that the use of change in global wall motion score index from low to peak dose dobutamine resulted in sensitivity of 83% and specificity of 71% for detection of coronary artery disease. In our study WMSI had lower sensitivity (62%) and higher specificity (88%) compared with Duncan's study. The sensitivity and specificity of WMSI in detecting CAD is lower than long axis function.

Mechanisms

The greater sensitivity of changes in long-axis function over WMSI might have several explanations. (1) The mitral ring gives rise to a strong echo, even when image quality is suboptimal,so that systolic amplitude and PWTD signals are simple to quantify even in patients with LBBB, thereby providing objective and reproducible measurements. In contrast, WMS analysis remains semiquantitative and dependent on operator experience. (2) A further advantage of long-axis assessment is that incoordinate long-axis shortening after aortic valve closure can be distinguished from

that during ejection, an assessment that is not possible with the repetition rate of 2-dimensional imaging.(3) Finally, the contrasting effects of stress in LBBB with or without ischemia meant that septal long-axis measurements performed particularly well in this group. This probably reflected their direct

Study Limitations

This is a single centre study with small number of patients. As in previous studies, patients with significant ventricular arrhythmias and atrial fibrillation which constitute important in both groups of cardiomyopathies, were not included. Strain-rate imaging might constitute another useful method for analyzing regional LV function in this setting, but this technique is not yet widely available, and its predictive accuracy in patients with LBBB has not been studied. It has been reported that patients with ischemic DCM more commonly have preserved right ventricular function and size compared with those with nonischemic DCM . In our study, the two groups of patients with did not have significantly different right ventricular size on echocardiogram. However, the response of the right ventricle to dobutamine was not analyzed.

Differentiating of ischemic and nonischemic cardiomyopathy solely on the basis of coronary angiography is imprecise because more than one process may be present simultaneously, i.e the association of DCM and coronary artery disease does not imply in all patients (especially in single vessel disease) that the DCM is ischemic in origin. Moreover, angiography does not provide a physiological assessment of severity of coronary artery disease.

Practical implications

Differentiation of ischemic from idiopathic dilated cardiomyopathy noninvasively is important in the prognostication . It reduce the need for invasive procedures and their attendant complications. Identification of ischemic cardiomyopathy by noninvasive methods is particularly important in planning further definitive management in such patients.

CONCLUSIONS

(1) Tissue Doppler Imaging during dobutamine stress is a simple, and effective non-invasive modality in differentiating ischemic from nonischemic dilated cardiomyopathy

(2) Blunted response to dobutamine identifies ischemic cardiomyopathy

(3) Tissue Doppler Imaging was especially useful in patients with left bundle branch block and dilated cardiomyopathy

(4) Tissue Doppler Imaging findings correlate well with coronary angiogram

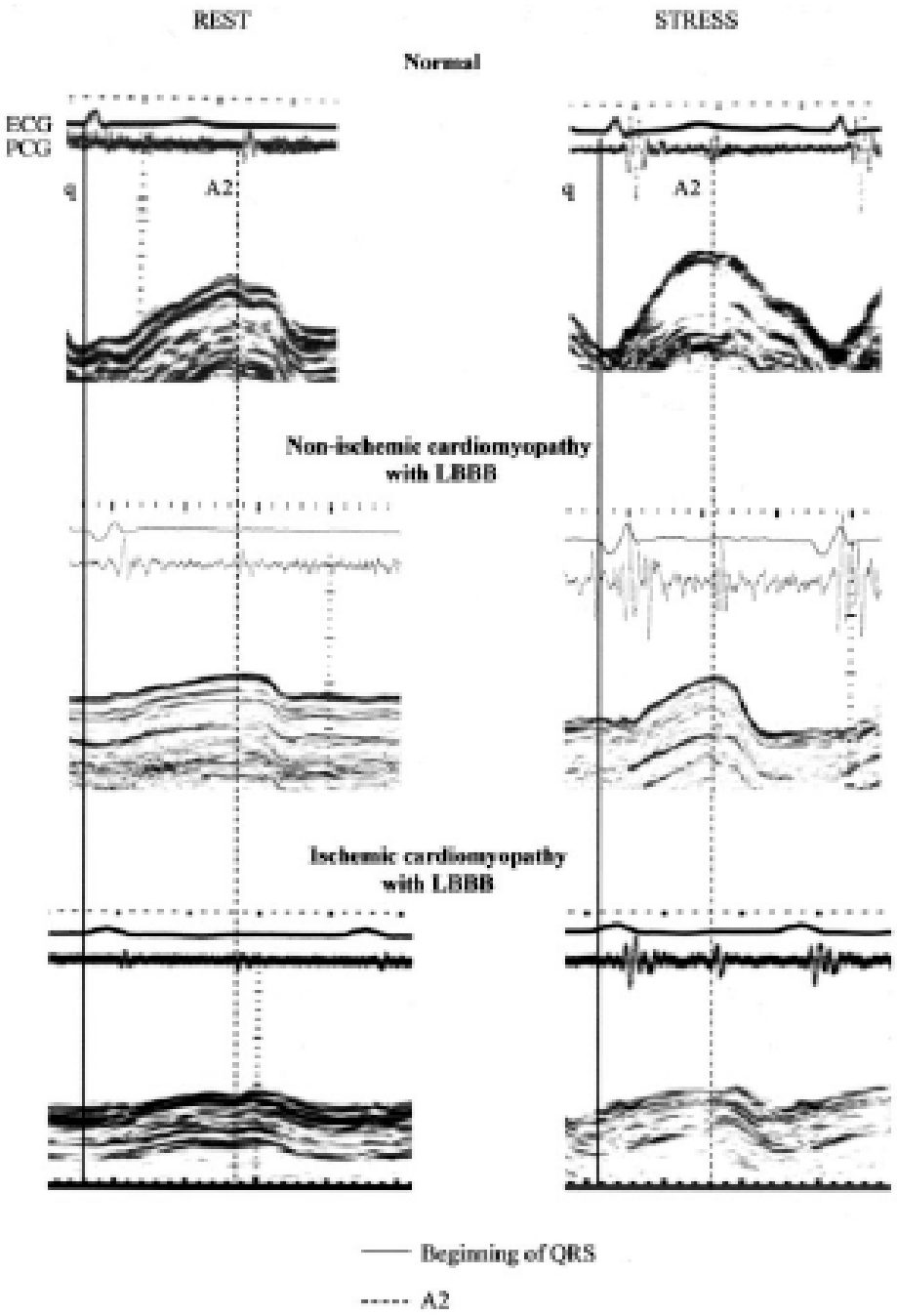


Figure 8. Top, Long-axis excursion normally increases with stress, and PES does not appear**. Middle**, In nonischemic cardiomyopathy and LBBB, amplitude is reduced at rest but increases with stress.**Bottom**, In ischemic cardiomyopathy and LBBB, amplitude is reduced and PES is present at rest, and neither changes with stress. PCG indicates phonocardiogram;A2, aortic valve closure; and q, Q wave of the ECG.

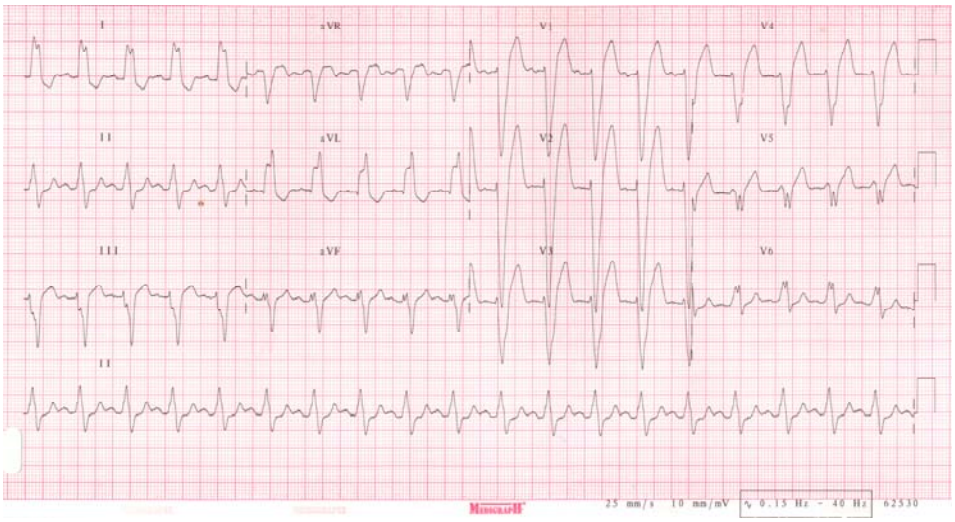


Figure - 9A ECG of a nonischemic DCM patient Mr. K shows LBBB

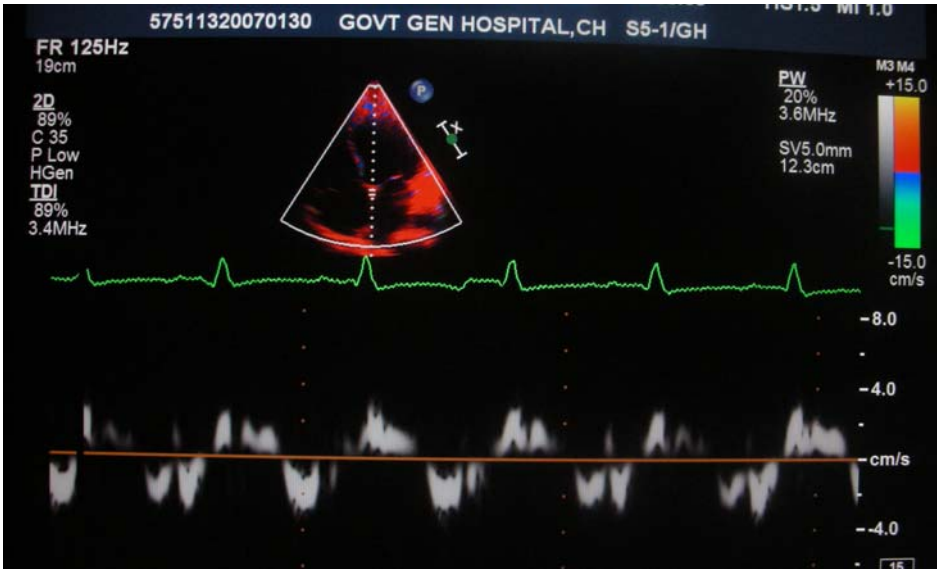


Figure - 9B. Pulsed Wave Tissue Doppler of mitral annulus of the same patient Mr. K **at rest** shows decrease in systolic and early diastolic velocity

Figure - 9C Pulsed Wave Tissue Doppler of mitral annulus of Mr. K **during Dobutamine** shows normal increase in systolic and early diastolic velocity

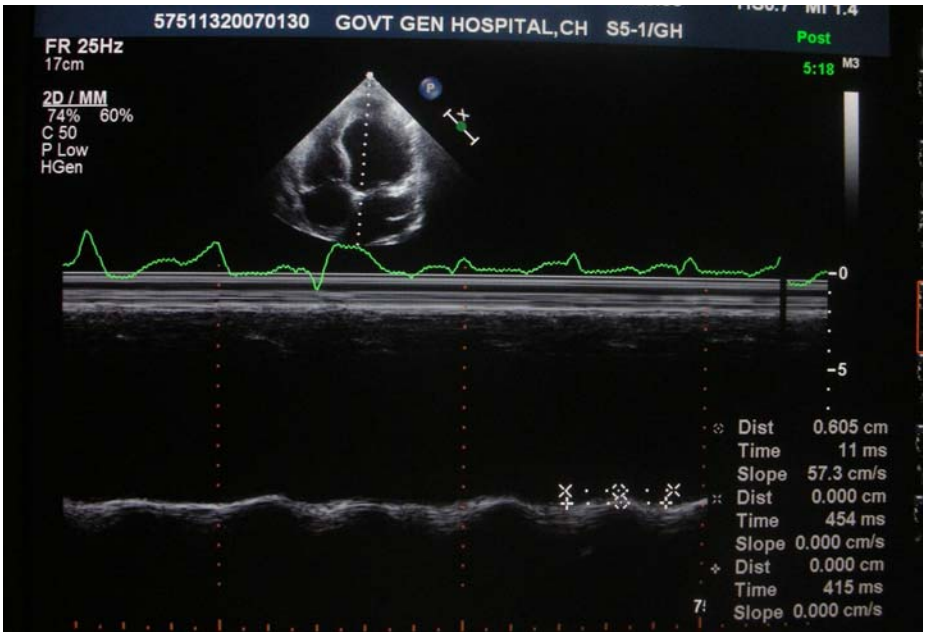


Figure - 9D. M-mode of mitral annulus Mr. K **at rest** shows decrease in systolic amplitude

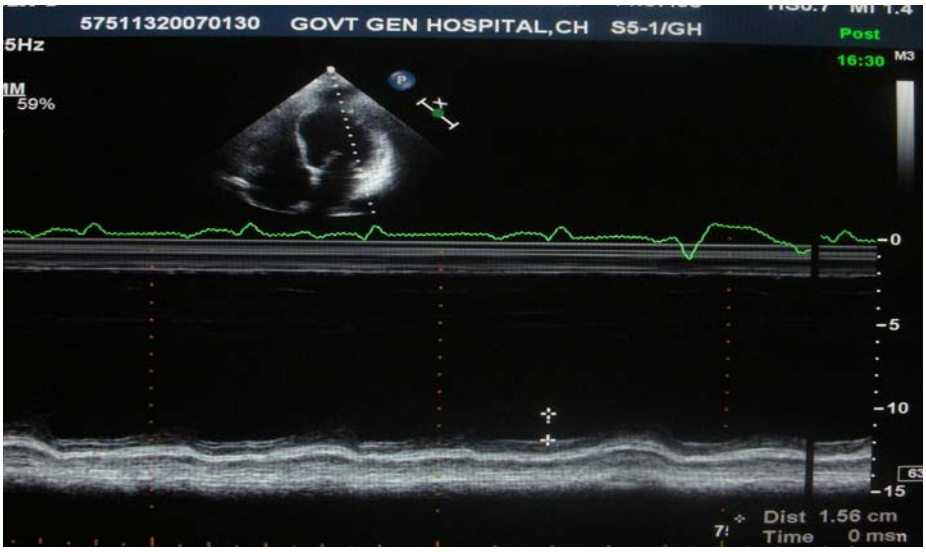


Figure -9E M-mode of mitral annulus Mr. K **at rest** shows decrease in systolic amplitude

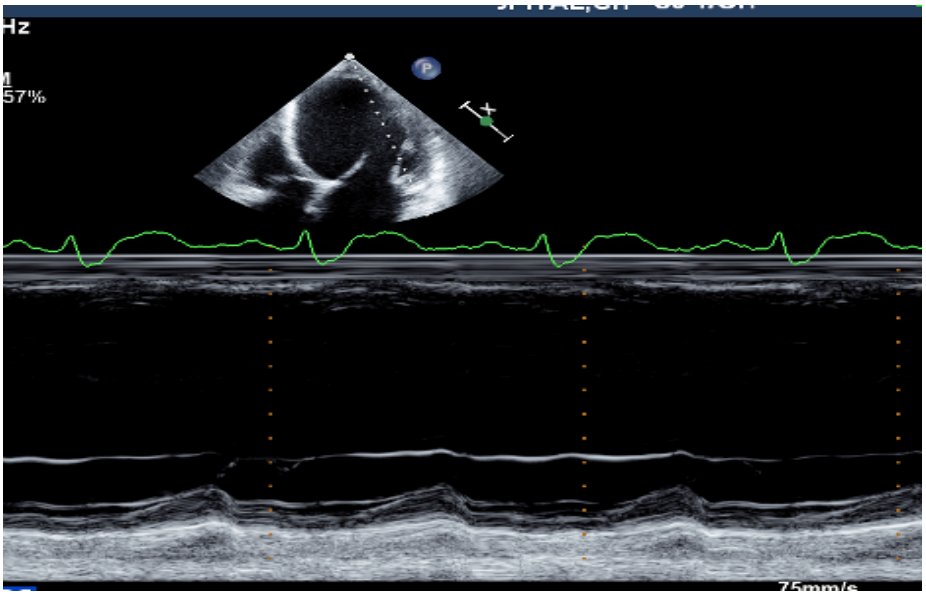


Figure -9F M-mode of mital annulus of Mr. K during peak dose **dobutamine** shows normal increase in systolic amplitude

RCA LCA

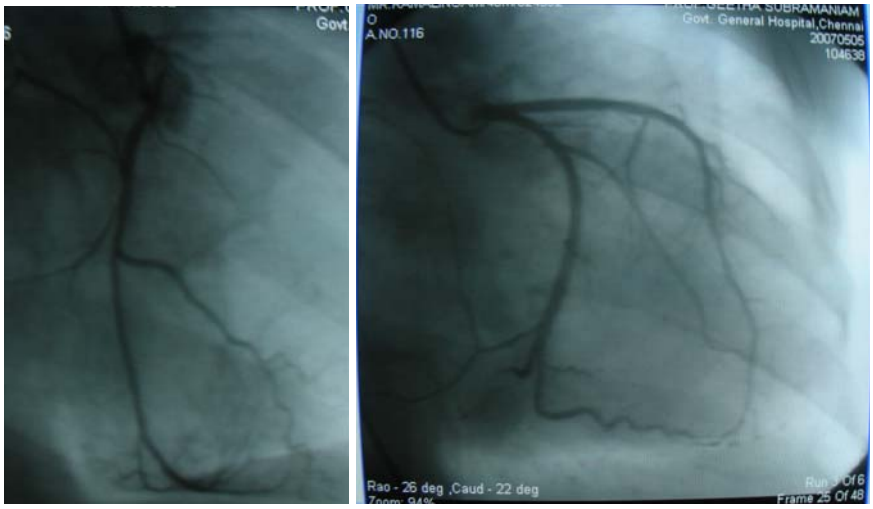


Figure - 9G. Coronary angiogram Mr. K shows normal epicardial coronary arteries

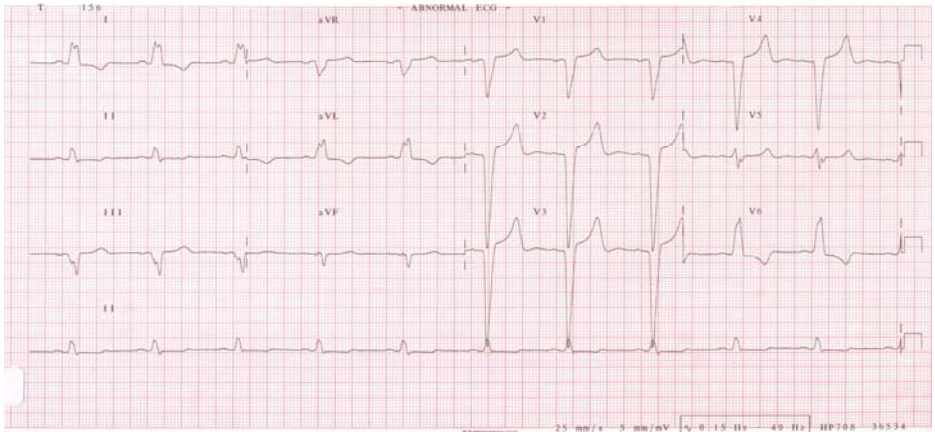


Figure - 10A. ECG of an Ischemic DCM patient Mr. R shows LBBB

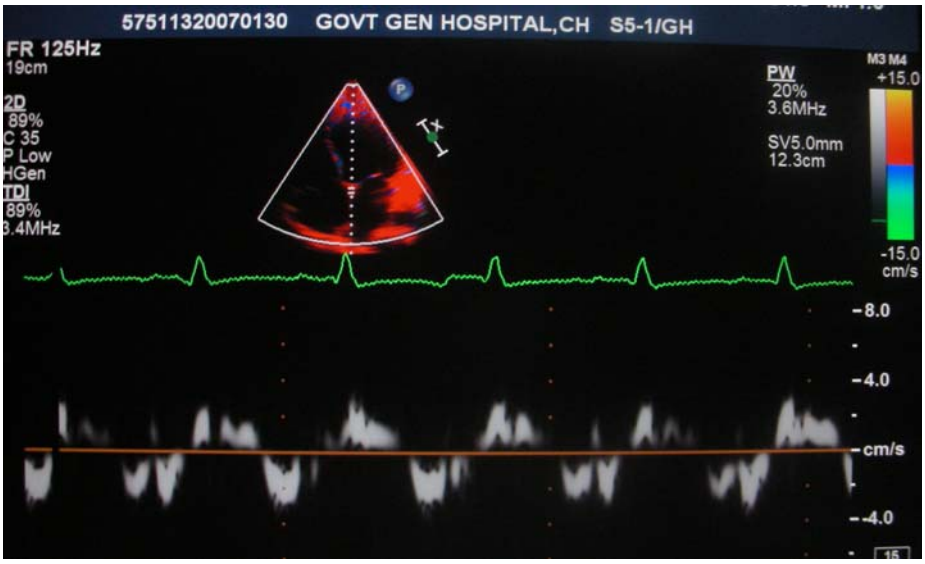


Figure – 10B. Pulsed Wave Tissue Doppler of mitral annulus of the same patient Mr. R **at rest** shows decrease in systolic and early diastolic velocity

Figure – 10C. Pulsed Wave Tissue Doppler of mitral annulus of Mr. R **during dobutamine Stress** shows blunted increase in systolic and early diastolic velocity

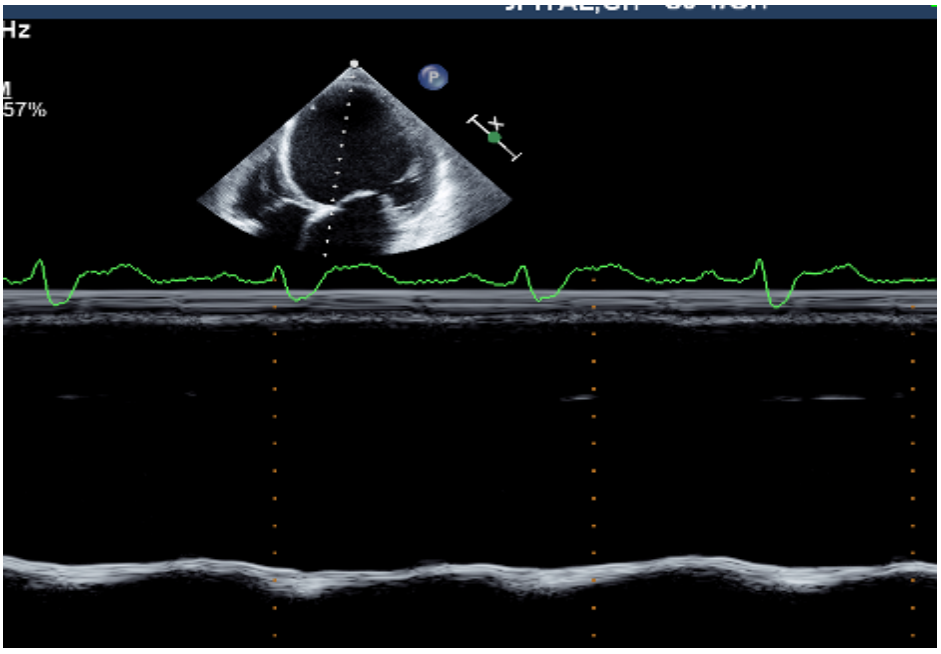


Figure - 10D. M-mode of mitral annulus Mr. R **at rest** shows decrease in systolic movement towards ventricle

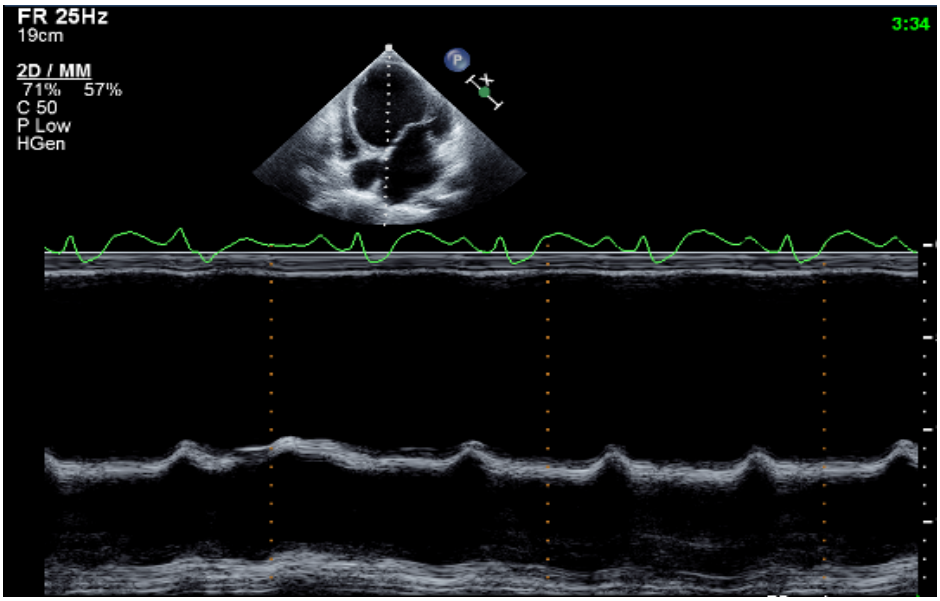


Figure - 10E. M-mode of mitral annulus Mr. R at peak **dobutamine** shows blunted increase in systolic excursion of annulus

RCA LCA

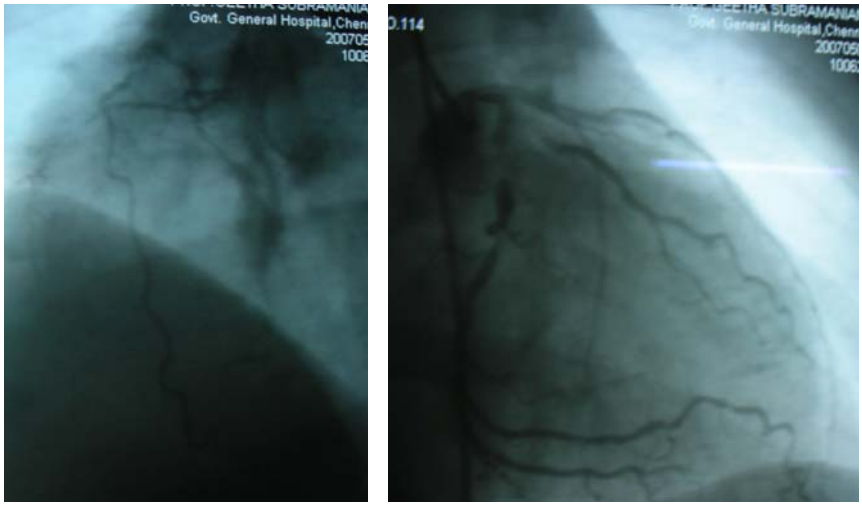


Figure - 10F. Coronary angiogram Mr. R shows three vessel disease

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PROFORMA

UTILITY VALUE OF TISSUE DOPPLER IMAGING DURING DOBUTAMINE STRESS IN DIFFERENTIATING ISCHEMIC FROM NONISCHEMIC DILATED CARDIOMYOPATHY

Patient name	:	Address	:
Age	:		
Sex	:	MRD NO.	:
Date	:	CD NO.	:

HISTORY

Chest pain	:	Dyspnea	:
Palpitation	:	Syncope	:
Pedal edema	:	Cough	:
H/O Prior MI	:	Rx details	:

RISK FACTOR ASSESSMENT

Hypertension	:	Diabetes	:
Dyslipidemia	:	Obesity	:
Smoking	:	Family CAD	:

EXAMINATION

Pulse rate	:	Blood pressure:	
JVP	:		

ELECTROCARDIGRAM

CHEST X RAY

ECHOCARDIOGRAPHY

Baseline Echocardiogram

Two dimensional :

M- mode :LVIDd- LVIDs -

Color flow :

Ejection fraction :

Tissue Doppler at rest

	Septal	lateral	posterior
1.Total amplitude, mm	-		
2.PES, mm	-		
3.Systolic amplitude, mm	-		
4.Systolic velocity, cm/sec	-		
5.Early diastolic velocity, cm/sec	-		

Dobutamine stress echocardiography(DSE)

Maximum dose required	-	Total dose infused	-
Atropine requirement	-	Peak heart rate / mt	-
Chest pain	-	Hypotension	-
Ventricular ectopics	-	V T	-
Death	-		

Tissue Doppler during DSE

	Septal	lateral	posterior
1.Total amplitude, mm	-		
2.PES, mm	-		
3.Systolic amplitude, mm	-		
4.Systolic velocity, cm/sec	-		
5.Early diastolic velocity, cm/sec	-		

LV contractility and 16-segments wall motion score index

1.At rest

2.During low dose dobutamine

3.During peak dose dobutamine

CORONARY ANGIOGRAM

Date :

CD NO :

LMCA -

LAD -

septals -

diagonals -

LCX -

RCA -

Collaterals -

Final Impression

DISCUSSION