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Original Article

Internal Medicine Section

Complementary Value of Tissue Doppler Imaging in Dobutamine Stress Echocardiography: A Prospective Cohort Study

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ABSTRACT

Introduction: In patients with Coronary Artery Diseases (CAD), the presence of viable myocardium predicts the recovery of Left Ventricular (LV) systolic function after revascularisation. The identification of myocardial viability during dobutamine stress echocardiography is subjective and with observer bias. Tissue Doppler Imaging (TDI) echocardiography has opened new possibilities for non-invasive quantification of myocardial function by directly interrogating myocardial velocity with high temporal and spatial resolution.

Aim: To determine the baseline regional myocardial and mitral annular Maximum Systolic Velocities (MSV) in patients with LV dysfunction and to compare the MSV values in viable and non-viable myocardium.

Materials and Methods: In this prospective cohort study, TDI of regional and annular LV myocardial velocities was performed at the baseline (at rest) in 352 patients with CAD and LV dysfunction who were referred for dobutamine stress Echocardiography. Viability assessment by 2 Dimensional (2D) methods was done simultaneously using routine dobutamine stress protocol. Patients were grouped in two groups based on the presence or absence of viability with 2D stress echocardiography. TDI velocities were compared in the two groups of patients with and without myocardial viability. Measurements of regional wall thickness, Ejection Fraction (EF) and Wall Motion Score Index (WMSI) were done to assess the regional and global LV function in these patients. Those patients who underwent revascularisation were subsequently assessed for functional recovery by 2D and TDI echocardiography before discharge from the hospital. Analyses were conducted using Statistical Package for Social Sciences (SPSS) version 16.0.

Results: The mean age of the patients was 58.2±8 years. Among 352 patients studied (124 females and 228 males), mean age 58 years (range 36 to 75 years). A total of 243 patients (69%) with viable myocardium as per 2D echocardiography had higher cut-off Baseline Regional Maximum Systolic Velocity (BRMSV) >0.03 m/s and baseline mitral annular systolic velocity >0.06 m/s with high sensitivity and specificity compared to patients with severe contractile dysfunction and non-viable myocardium.

Conclusion: Tissue doppler parameters like regional myocardial systolic and mitral annular velocities have shown significantly higher cut-off values in those patients with ischaemic and viable myocardium compared to non-viable myocardium.

Keywords: Mitral annular velocity, Regional maximum systolic velocity, Viable myocardium

INTRODUCTION

Qualitative and semi quantitative evaluations of myocardial function by 2-D and M-mode echocardiography have long been the most important non-invasive methods for diagnosing CAD [1,2]. The hibernating myocardium denotes to resting LV dysfunction due to reduced coronary blood flow that can be somewhat or completely reversed by myocardial revascularisation and by reducing myocardial oxygen demand [3,4]. Identification of ischaemic and viable myocardium has important prognostic and therapeutic implications as significant recovery of function occurs after revascularisation [5].

Ischaemic and hibernating myocardium may appear as wall motion abnormalities in 2D echocardiography [6] and have a positive inotropic reserve which can be stimulated by catecholamine in contrast to irreversibly damaged myocardium. Stress echocardiography aims at detecting a stimulated positive inotropic response in segmental wall motion. In the clinical setting of CAD and LV dysfunction, prediction of LV functional improvement after revascularisation is done by using various methods like nuclear scanning, cardiac Magnetic Resonance Imaging (MRI) and dobutamine stress echocardiography [7,8]. Scintigraphic studies with Fluorodeoxyglucose Positron Emission Tomography (FDG PET) and thallium-201 have demonstrated accurate results in the detection of viability and the prediction of LV recovery [9,10]. FDG PET is currently reputed to be the most sensitive [11,12]. Being low cost, dobutamine stress echocardiography which is based on 2D visual assessment of the examiner is the most frequently used stress echocardiographic test for detection of myocardial viability. Infusion of dobutamine at rates of 5 to 20 μg/kg/minutes is used to detect myocardial viability. Though dobutamine stress echocardiography is a frequently used and valuable tool for the evaluation of ischaemic myocardium, its interpretation still remains subjective, relying on image quality and sonographer's experience [13,14].

TDI permits assessments of myocardial velocities which may reflect regional myocardial function by using frequency shift of sound waves [15]. TDI echocardiography has opened new possibilities for non-invasive quantification of myocardial function by directly interrogating myocardial velocity with high temporal and spatial resolution [16]. Regional myocardial systolic velocity can be low in infarcted myocardium compared to viable and ischaemic zones. In Studies by Kalra DK et al., and Shan K et al., Peak systolic velocity (Sm) and early diastolic velocity (Em) were significantly higher in normal segments. Previous researches have demonstrated peak myocardial velocities in normal myocardium without much work on infarcted muscle [17,18]. Measurement of these regional velocities can offer an objective means to quantify global and regional LV function and to improve the accuracy and reproducibility of conventional echocardiography. The present study was designed to investigate how velocity patterns in ischaemic and infarcted myocardium relate to regional function at rest. It tests whether quantitative DTI provides information regarding the regional myocardial systolic function and compares the values in those with and without viability by 2D dobutamine stress echocardiography. It aimed to evaluate the sensitivity and specificity of the TDI parameters for the detection of viable myocardium.

MATERIALS AND METHODS

This was a prospective cohort study conducted from 1st January to 30th June 2015 conducted on patients undergoing dobutamine stress echocardiography at the Department of Cardiology, Government Medical College, Kottayam, and Kerala, India. The study was approved by the Institutional Ethics Committee (IEC) (SBMR- IRC 05/2014).

Inclusion criteria: Patients aged between 18-75 years with CAD and LV dysfunction, classified according to New York Heart Association (NYHA) functional class I, II, and III [20] were included in the study.

Exclusion criteria: Patients classified as NYHA functional class IV, those with significant arrhythmia, Myocarditis or Valvular/congenital heart disease were excluded from the study.

Sample size calculation: Sample size was calculated from a Pilot study conducted with 50 cases, the prevalence of viable myocardium in patients undergoing stress echo was 35% [19]. In order to detect a difference of 0.25 between the proportions of acceptable intubating conditions per group, with 80% power and 5% level of significance, 352 patients were included.

Study Procedure

After consent from patients, and applying inclusion criteria and exclusion criteria, patients with CAD and LV dysfunction were taken up for the study. History was taken and a clinical examination was done. A 2D assessment of regional wall motion and M-mode assessment for regional wall thickness and EF were done. Regional Wall Motion Score Index (RWMSI), and Ejection Fraction (EF) were calculated at rest [21]. TDI was performed at the baseline. Baseline Annular Maximum Systolic Velocity (BAMSV) and BRMSV were measured by placing the cursor at medial and lateral annulus (average of the 2 was taken) and at two points where the myocardium appears hypocontractile (average of the two was taken).

Viability assessment by 2D methods was done simultaneously using routine dobutamine stress protocol. Dobutamine was infused at rates of 5 to 20 µg/kg/minutes [22]. Patients were grouped in two groups (243 patients had viable myocardium and 109 had non-viable myocardium) based on the presence or absence of viability with 2D stress echocardiography. TD velocities were compared in the two groups of patients with and without myocardial viability by 2D dobutamine stress. Those patients who underwent revascularisation by Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG) based on their symptoms and 2D viability findings were subsequently underwent 2D and TDI and measured the Regional Maximum Systolic velocity post-procedure (RMSVP) to assess the functional recovery before discharge from the hospital.

STATISTICAL ANALYSIS

Data was entered in Microsoft Excel and data analysis was performed using Statistical Package for Social Sciences (SPSS) version 16.0. Normality of the data was assessed by Kolmogorov-Smirnov test. The comparison of quantitative variables between the two groups were analysed by independent sample t-test. Association between categorical variables was analysed by the Chi-square test. Receiver Operating Characteristic (ROC) curve was plotted Area Under Curve (AUC). Variables that were found significantly associated with the dependent variables were subjected to multivariate analysis. ROC curve of predicted probability of the Binary logistic regression model for VIB 2D was made.

RESULTS

Among 352 patients studied 124 were females and 228 were males with the mean age 58.2±8 years [Table/Fig-1]. There was significant association between DM, HTN, CAD CSA, CAD ACS, PTCA and CABG and 2D viability [Table/Fig-2].

Parameters		Frequency n (%)
Gender	Male	228 (64.8)
	Female	124 (35.2)
Smoking		152 (43.2)
DM		213 (60.5)
HTN		198 (56.3)
CAD CSA		170 (48.3)
CAD ACS		277 (78.7)
DLP		246 (69.9)
VIB 2D		243 (69)
FUN REC		253 (71.9)
PTCA		245 (69.6)
CABG		25 (7.0)

[Table/Fig-1]: Baseline Characteristics.
DM: Diabetes mellitus; HTN: Hypertension; CAD CSA: Coronary artery disease chronic stable angina; ACS: Acute coronary syndrome; DLP: Dyslipidaemia; VIB 2D: Viability 2 dimensional; FUN REC: Functional recovery; PTCA: Percutaneous trans luminal coronary artery; CABG: Coronary artery bypass graft

Variable		VIB 2D No N	VIB 2D Yes N	Total N	χ^2	p-value
DM	No	62	77	139	20.0	**<0.001**
	Yes	47	166	213		
HTN	No	19	135	154	44.4	**<0.001**
	Yes	90	108	198		
CAD CSA	No	74	108	182	16.6	**<0.001**
	Yes	35	135	170		
CAD ACS	No	7	68	75	20.9	**<0.001**
	Yes	102	175	277		
PTCA	No	88	19	107	189.1	**<0.001**
	Yes	21	224	245		
CABG	No	108	219	327	9.2	**0.002**
	Yes	1	24	25		

[Table/Fig-2]: Association of baseline characteristics with 2D viability.
χ^2 test was done; 'p' significance level is <0.05; Bold p-values are significant

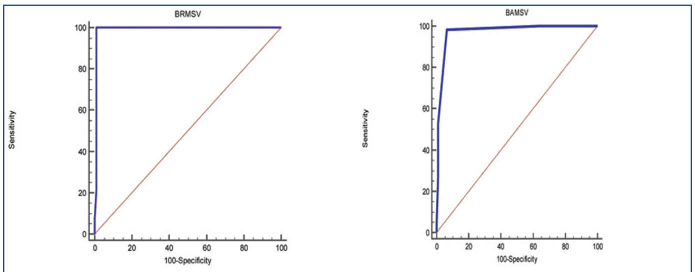
In the present study, mean RWMSI was 1.66 in patients with viable myocardium compared to 2.69 in those with non viable myocardium; p<0.001 [Table/Fig-3].

Variables	VIB 2D No Mean±SD	VIB 2D Yes Mean±SD	t-value	p-value
RWMSI	2.69±0.32	1.66±0.28	30.485	**<0.001**
EF	29.14±3.44	43.29±22.72	6.465	**<0.001**
RWTHI	4.46±0.55	6.61±0.86	23.985	**<0.001**
BRMSV	0.026±0.006	0.053±0.007	36.048	**<0.001**
BAMSV	0.057±0.008	0.086±0.018	15.674	**<0.001**
RMSV P	0.028±0.011	0.055±0.008	25.8	**<0.001**

[Table/Fig-3]: Association of echocardiographic parameters with 2D viability.
t-test done; 'p' significance level is <0.05, (RWMSI: Regional wall motion score index; EF: Ejection fraction; RWTHI: Regional wall thickness; BRMSV: Baseline regional maximum systolic velocity; BAMSV: Baseline annular maximum systolic velocity; RMSV P: Baseline regional maximum systolic velocity post procedure)

Two hundred and forty five patients underwent PCI and 25 patients underwent CABG and 82 patients did not undergo revascularisation and were rejected in view of their irreversible LV dysfunction. Of these 270 patients who underwent revascularisation 253 (93.7%) had functional recovery.

From the AUC of ROC, optimum cut-off BRMSV >0.03 m/s sensitivity 100, Specificity 99.08, positive predictive value (+PV 99.6) and negative predictive value (-PV100). Optimum cut-off BAMSV >0.06 m/s Sensitivity 98.35 Specificity 93.58+PV97.2 and -PV96.2 [Table/Fig-4].



	AUC	SE	95% CI
BRMSV	0.992	0.008	0.976 to 0.999

	AUC	SE	95% CI
BAMSV	0.974	0.010	0.952 to 0.988

[Table/Fig-4]: ROC curve of tissue doppler parameters to predict VIB 2D.

There were significant positive correlations of BAMSV between the RWTs and EF in those with viable myocardium, and negative correlation with WMSI, indicated by the r values as shown in [Table/Fig-5].

Correlation of BAMSV with other variables	Pearson correlation coefficient r	p-value
RWMSI	-0.540	**<0.001**
EF	0.616	**<0.001**
RWTHI	0.807	**<0.001**
BRMSV	0.678	**<0.001**
RMSV P	0.597	**<0.001**

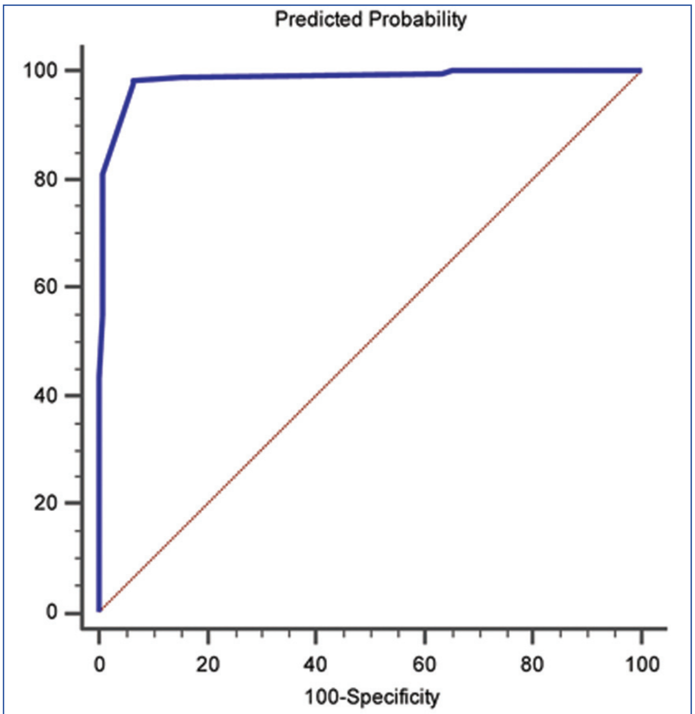
[Table/Fig-5]: Correlation of BAMSV.

Correlation was assessed for only for BAMSV. BRMSV values were similar and hence correlation assessment was not possible. There are only small differences between the values among the non viable group with regard to RMSV. In the binary logistic regression model for viability viable myocardium group had significant p-value in terms of BAMSV and also with dyslipidaemia [Table/Fig-6].

Variables	b-value	SE	Wald	df	p-value	OR	95% CI for OR	
							Lower	Upper
BAMSV	8.187	1.217	45.23	1	<0.001	3594.2	330.7	39066.1
DM	0.706	0.934	0.572	1	0.45	2.0	0.3	12.6
HTN	0.485	0.848	0.327	1	0.568	1.6	0.3	8.6
DLP	3.27	1.191	7.533	1	0.006	26.3	2.5	271.8
Constant	-6.7	1.624	17	1	0.001	0.0		

[Table/Fig-6]: Binary logistic regression model for VIB 2.
Statistically feasible parameters are considered for logistic regression analysis. Other ones were not suitable
SE: Standard error; OR: Odds ratio; CI: Confidence interval

Area under the ROC curve (AUC) 0.984; Standard error 0.006; 95% Confidence interval 0.965 to 0.994; z statistic 77.67; Significance level P (area=0.5) <0.0001 (For a given cut-point in a prediction model or score, the mean of sensitivity and specificity equals the AUC). [Table/Fig-7]. Sensitivity and specificity 98.4%; Standard error 0.006; 95% Confidence interval 0.965 to 0.994; z statistic 77.67; Significance level P (area=0.5) <0.0001



[Table/Fig-7]: ROC curve of predicted probability of the binary logistic regression model for VIB 2D.

DISCUSSION

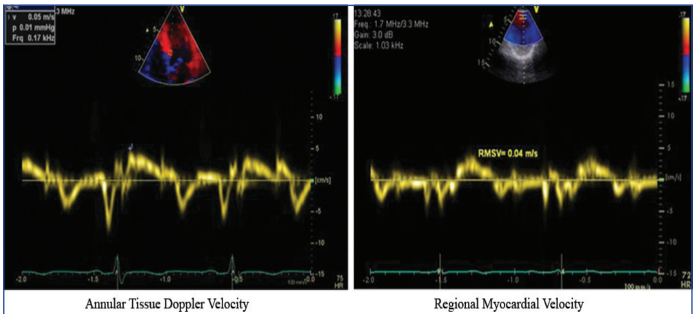
Tissue doppler parameters like regional myocardial systolic and mitral annular velocities has shown significantly higher cut-off values in those patients with ischaemic and viable myocardium compared to non-viable myocardium. It complements the standard interpretation of stress echocardiograms. Mean and SD of BRMSV in patients with and without viable myocardium was 0.053±0.007; 0.026±0.006 (t: 36.048 p<0.001). Similarly mean and SD BAMSV is 0.057±0.008; 0.086±0.018 (t: 15.674 p<0.001). The present study, however, demonstrates importance of peak systolic velocity to serve as a quantitative marker of regional function. The ability of peak regional velocity to serve as a quantitative marker of regional function was confirmed in the ischaemic and viable myocardium with higher cut-off values using ROC. A number of studies have confirmed the diagnostic potential of TDI in the assessment of regional myocardial function [23-25]. In the present study, the peak myocardial velocity value in non-ischaemic myocardium showed satisfactory agreement. In a study by Voigt JU et al., 25 normal subjects were observed at rest using parasternal and apical methods [26]. Peak maximal velocity value was 0. 37±0.29 cm/sec.

WMSI was calculated for the entire left ventricle and for each vascular territory using the sum of individual scores divided by the respective number of segments. A WMSI of 1.0 (16/16) is considered normo kinetic. WMSI of 1.5, 2.0, 2.5 and 3 are designated mild hypokinesia, hypokinesia, severe hypokinesia and akinesia, respectively [27]. RWMSI mean±SD in patients with and without viable myocardium are 1.66±0.28; 2.69±0.32 (p<0.001). In the present regional wall thickness at end diastole was low in infarcted myocardium compared to the viable and ischaemic myocardium. The normal range myocardial thickness is 0.6-1.0 cm LV posterior wall end diastole. Patients with non-viable and ischaemic myocardium will be having high WMSI and low myocardial thickness, as well as, low cut-off values of myocardial systolic velocities. Myocardium with thick infarct (>50% transmurality) undergoes wall thinning during contraction as opposed to healthy myocardium. In the present study, mean±SD of regional wall thickness in patients with and without viable myocardium are 6.61±0.86; 4.46±0.55 (p<0.001), EF mean±SD 43.29±22.72; 29.14±3.44 (p<0.001). In a study by Walpot J et al., normal values LV mid-diastolic wall thickness from coronary CT angiography found that the LV was thickest in the basal septum with a mean thickness of 8.3 mm and 7.2 mm and thinnest in the midventricular anterior wall with 5.6 mm and 4.5 mm for men and women, respectively [28].

The present findings indicate that the diagnostic power of dobutamine stress echocardiography may be improved by measuring maximum systolic and mitral annular velocities. In actively contracting myocardium, the peak systolic velocity measured during LV ejection reflected changes in myocardial function. In severely ischaemic and dyskinetic myocardium, however mitral annular velocities were the better markers of myocardial dysfunction. TDI parameters namely baseline mitral annular velocity showed a positive correlation with viable myocardium of 2D stress echocardiography. Together with WMSI and RWTHI tissue doppler velocities complement the prediction of viable myocardium to the dobutamine stress echocardiography.

Qualitative and semi quantitative evaluations of myocardial function by 2D and M-mode echocardiography have long been the most important non-invasive methods for diagnosing CAD. TDI is a potentially powerful method for diagnosing myocardial ischemia and infarction and has been introduced as a method to quantify myocardial function in terms of tissue velocities and ischaemic regions are characterised by a decrease in systolic velocities at rest or during stress echo [15,23].

The clinical implementation of TDI, however, has been relatively slow, and most echocardiographic laboratories do not apply TDI as a routine diagnostic method. This may in part be attributed to a lack of established criteria for how to analyse and interpret the TDI velocity trace, which reflects the relatively limited insight into the aetiology of the different velocity components. Timing of TDI velocities in relation to the different cardiac phases should be possible by simultaneous display of myocardial velocities, ECG, and aortic and mitral valve signals [24]. Systolic velocities are directed upwards and diastolic velocities are directed downwards (e' and a' early and late myocardial velocities). [Table/Fig-8] is the example showing TDI of a patient from the laboratory.



[Table/Fig-8]: Pulsed wave Tissue Doppler Imaging (TDI) of the LV peak myocardial systolic velocity.

Pulsed-wave tissue doppler recording of myocardial velocities in the LV anterior mid-wall. Systolic velocities are directed upwards and diastolic velocities are directed downwards.

Myocardial doppler velocities correlated well with 2D echocardiography as measured by dobutamine stress confirming that TDI velocities reflect regional myocardial motion [25]. The use of inotropic agents (epinephrine and isoproterenol) it was documented that resting wall motion abnormalities may improve and that this improvement was predictive of subsequent improvement with coronary bypass surgery [29]. In the present study, Regional Myocardial systolic velocity post-coronary angioplasty (RMSVP) showed positive correlation with BAMSV. The mean and standard deviation of RMSVP was 0.028±0.011 in patients with viable myocardium and 0.055±0.008 (t:25.8 p<0.001). This analysis includes measurement of myocardial velocities at the regions or reduced wall motion and basal mitral annular tissue in addition to 2D findings. Furthermore, a more comprehensive analysis of the myocardial Doppler velocity signal may progress the ability of TDI to recognise ischaemic myocardium.

Limitation(s)

The measurements of absolute velocities are angle dependent, and one should be aware of this limitation. The problems with cardiac translation and rotation are inherent in all TDI techniques. In the present study, standard 2-chamber and short axis views were used and no attempt was made to correct for angle dependency of TDI measurements. Myocardial ejection velocities had very low amplitudes and appeared to be influenced by tethering effects and/or translational motion.

CONCLUSION(S)

Diagnostic power of dobutamine stress echocardiography may be improved by measuring maximum systolic and mitral annular velocities. In actively contracting myocardium, the peak systolic velocity measured during LV ejection reflected changes in myocardial function. In severely ischaemic and dyskinetic myocardium, however, mitral annular velocities were the better markers of myocardial dysfunction. TDI parameters namely baseline mitral annular velocity showed a positive correlation with viable myocardium of 2D stress echocardiography. Together with WMSI and RWTHI, tissue doppler velocities complement the prediction of viable myocardium to the dobutamine stress echocardiography.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
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