ECHOCARDIOGRAPHIC ASSESSMENT OF INTER AND INTRA VENTRICULAR DYSSYNCHRONY IN HEART FAILURE PATIENTS WITH NORMAL QRS DURATION

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CERTIFICATE

This is to certify that the dissertation titled "**ECHOCARDIOGRAPHIC ASSESSMENT OF INTER AND INTRA VENTRICULAR DYSSYNCHRONY IN HEART FAILURE PATIENTS WITH NORMAL QRS DURATION"** is the bonafide original work of Dr**. T.VISWANATHAN**, 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 2014.The period of post-graduate study and training was from August 2011 to July 2014.

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DECLARATION

I, **Dr.T.VISWANATHAN**, solemnly declare that this dissertation entitled, "**ECHOCARDIOGRAPHIC ASSESSMENT OF INTER AND INTRA VENTRICULAR DYSSYNCHRONY IN HEART FAILURE PATIENTS WITH NORMAL QRS DURATION**" is a bonafide work done by me at the department of Cardiology, Madras Medical College and Government General Hospital during the period 2011 – 2014 under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital, Professor M.S.Ravi 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**.

Place: **SIGNATURE OF THE CANDIDATE**

Date :

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CONTENTS

INTRODUCTION

The management of patients with heart failure is an important issue in cardiology. The cost of healthcare associated with management and hospitalization is substantial. Device therapy for patients refractory to medical therapy focuses on improving the clinical outcome and quality of life.

Normally Electrical activation and conduction through the His Purkinje network occurs fast. This results in synchronous mechanical contraction of the heart. Many diseases of the heart produce changes in the temporal sequence of early and late systolic contraction of different regions of the myocardium[1]. This results in abnormal contraction pattern due to the resultant electromechanical dyssynchrony. This causes an increase in the duration of QRS on ECG.

Some studies report mechanical dyssynchrony in a subgroup of patients with diastolic heart failure[2] too. Dyssynchrony has also been reported in some patients with heart failure and decreased ejection fraction and a normal QRS duration[3].

The differential regional activation and dyssynchronous left ventricular contraction by decreasing ejection and relaxation has the net effect of reduced cardiac output. Work efficiency of the myocardium is also decreased because of the dyssynchrony[1].

Heart failure is associated with alterations in the local and systemic neuro hormonal milieu playing an important role in pathological remodeling and changes at the cellular level[1,4]. Superimposition of electrical conduction delay and mechanical dyssynchrony over this setting results in additive effects and creates complex pathological changes and increased propensity to arrhythmias[1].

Cardiac dyssynchrony can beatrioventricular, interventricular, and intraventricular. Among these, intraventricular dyssynchrony has the greatest effect on contractile impairment. Cardiac resynchronization therapy affects intraventricular dyssynchrony predominantly[5].

Presently Cardiac resynchronization therapy is recommended in heart failure patients with symptoms refractory to medical treatment, decreased LV ejection fraction and QRS duration more than 120 milliseconds. Focused update (2010) of ESC guidelines for device therapy in heart failure recommends CRT for NYHA function class III/IV, LVEF $\leq 35\%$ and QRS ≥ 120 ms, despite Optimal medical therapy (CLASS 1 A recommendation)[6]

This is based on the assumption that widened QRS is a marker of alterations in the structure responsible for cardiac dyssynchrony. Several studies have documented that with increase in the severity of heart failure, widening of QRS

occurs. Widened QRS has also been associated with increased mortality in patients with LV failure.[7]

However, the relationship of QRS duration to mechanical dyssynchrony may not be parallel as documented by several studies[8,9]. Many heart failure patients with narrow QRS (120ms) may have significant dyssynchrony. On the other hand not all patients with LBBB may show correlation between the QRS duration and the magnitude of mechanical dyssynchrony.

Cardiac resynchronization therapy and its benefits in heart failure is based on resynchronizing the different regions so that the effects of dyssynchrony are modified.

Based on the current guidelines, nearly 30% of the patients do not respond as expected to CRT. About 40% of patients do not demonstrate the reverse remodeling of LV after CRT[10].

Assessment of dyssynchrony is useful in selecting patients. This may be potentially beneficial in assessing those patients with a narrow QRS complex and mechanical dyssynchrony.

The issue whether CRT based on dyssynchrony would add to the outcomes was examined in the ECHO-CRT study which was terminated prematurely because

of increased mortality[11]. On the basis of data available currently guidelines do not recommend CRT for patients with narrow QRS.

Assessment of Dyssynchrony can be done using various modalities. These include M MODE Echocardiography, Tissue Doppler imaging, deformation imaging using color Tissue Doppler or two-dimensional speckle tracking and velocity encoded MRI[12].

Strain imaging is shown to be correlated with outcomes. But the sensitivity, specify are suboptimal. Tissue Doppler imaging despite limitations can be used in the assessment if carefully done[12].

Several indices have been used for the dyssynchrony assessment using TDI[12]. These include difference of more than 40 ms between aortic and pulmonary pre ejection times for assessing interventricular dyssynchrony. For intraventricular electromechanical dyssynchrony, they include septal to posterior wall delay, septal to lateral wall delay, dyssynchrony index and difference between the times to peak systolic velocity (Ts) of 12 LVsegments.

Intraventricular dyssynchrony occurs in heart failure with diverse etiologies. Apart from ischemic causes other conditions include heart failure associated with

chronic kidney disease[13], Valvular heart diseases (Mitral Regurgitation) and Toxins.

In the present study we propose to assess the prevalence of inter and intraventricular dyssynchrony in heart patients with normal QRS duration irrespective of the etiology.

AIMS & OBJECTIVES

To assess the prevalence of inter and intraventricular dyssynchrony in patients with heart failure and Normal QRS duration echocardiographically using M mode and Tissue Doppler imaging (TDI).

REVIEW OF LITERATURE

Patients with Heart failure show dyssynchrony. However, even in normal hearts, the contraction is not uniform. This is due to the complex arrangement of ventricular fibers. Hence it is useful to know the normal myocardial architecture to understand the mechanisms responsible for dyssynchrony.

Normal Myocardial fiber Architecture

Helm et al[14] using Tensor magnetic imaging has shown that there are two types of myocardial fiber architecture. In the endocardium and the epicardium the fibers are arranged longitudinally and in the midwall they are oriented circumferentially. These change from one direction to another. Different myocardial regions have to be activated temporally because of this nature of the architecture. Also the myocardial fibers between the endocardium and epicardium show temporal activation.

A similar thing exists between apex and base. This is due to the disparity in electrical activation of different regions by the His Purkinje system. The electrical wave front produced proceeds from apical region and endocardium to the basal region and epicardium. Because of this the electrical activation in different regions may differ by as much as 80 to 100 millisec. However this type of temporal activation of myocardial fibers helps in effective pump function.

Mechanisms of Dyssynchrony

Dyssynchrony can occur because of two mechanisms[15]. In the setting of LBBB there is a temporal delay in activation of different segments of heart. Septal activation occurs first and the lateral wall is the last part to be activated by intra myocardial conduction. This results in electromechanical delay resulting in dyssynchrony. The other mechanism operates when dyssynchrony occurs with abnormal loading conditions of the heart. Here the electrical activation is normal.

Yano et al[16] showed that dyssynchrony can be induced by clamping the aorta in dogs producing increased afterload. Studies by Wang et al showed that diuretics and vasodilators can improve dyssynchrony in heart failure[17].

The second type of dyssynchrony due to abnormal loading conditions may be part heart failure itself. Resynchronization will not be useful in this setting.

Effects of dyssynchrony in heart failure[1]

Conduction defects are commonly observed in heart failure. This includes left bundle branch block. There is delayed activation of left basal posterolateral

segment of LV. When the septum which is activated early contracts the lateral free wall does not participate in the contraction whereas in late systole the lateral wall because of the delayed intra myocardial activation contracts. But the septum is in a state of relaxation leading to stretch. The net result of these uncoordinated contractions results in decreased force generation, delay in LV pressure rise (dp/dt) and resultant decreased cardiac output. Adding to this, postero lateral papillary muscle may also have delayed activation. The resulting mitral regurgitation further worsens the output.

Apart from decreased LV function, efficient myocardial work is also reduced. The lateral wall has higher stretch and therefore has more stress. Blood flow differences in different work loaded regions may in addition contribute to heart failure.

Byrne et al[5]. Showed that there is less dyssynchrony in RBBB compared to LBBB. This difference mainly because of the lack of symmetry in left ventricular geometry. In RBBB the effect of cardiac resynchronization therapy is minimal. The causes of this are the lesser degree and the different pattern of dyssynchrony.

Molecular changes in dyssynchrony

Several molecular changes occur in heart failure patients with dyssynchrony. These are in addition to the alterations in the neuro hormones in the setting of heart failure. There occurs differential protein expression in different regions of the heart. These changes occur with vital kinases at the cellular level. Spragg et al[4]. showed important differences in the proteins associated with calcium transport across different regions in a canine model. Compared to controls without dyssynchrony, the levels of SERCA, Phospholamban and gap junction protein connexin 43 were found to be low. This was associated with increased levels of mitogen activated kinase. This was observed in the lateral wall than the septum. The study by Vanderheyden et al[18] in CRT responders supports this. The implications of altered expression of gap junction proteins is an increase in the susceptibility to develop arrhythmias by increasing action potential duration.

Also dyssynchrony causes downregulation of mediators involved in cell survival signaling[4].

TYPES OF DYSYSNCHRONY

Altered cardiac synchrony can exist between the atria and the ventricles (atrioventricular) between the two ventricles (interventricular) and between different regions of the left ventricle (intraventricular).

For recording Atrioventricular dyssynchrony pulsed-wave Doppler echocardiographic recording of Transmitral inflow is performed. The diastolic filling ratio is arrived at by the ratio of filling time in diastole is calculated by adding the total duration of E and A wave. This divided by the RR interval gives the diastolic filling ratio. If the ratio is less than 40% notable atrioventricular dyssynchrony is present[12]. In The multi center PROSPECT[19] trial individual echocardiographic parameters were assessed to measure predictors of CRT. AV dyssynchrony as assessed by LVFT / RR ratio had only modest value in predicting response to CRT.

INTERVENTRICULAR DYSSYNCHRONY

The dyssynchrony between the left and the right ventricle is referred to as interventricular dyssynchrony. Either pulsed wave Doppler or Tissue Doppler imaging can be employed to assess it[12].

Pulsed wave Doppler sampling proximally to the aortic and pulmonary valves are obtained .The pre ejection time of RV and LV are assessed by the time interval between the onsets of QRS to the onset of ejection. Significant interventricular dyssynchrony exists if the difference between the aortic and

pulmonary pre ejection times is more than 40 ms.

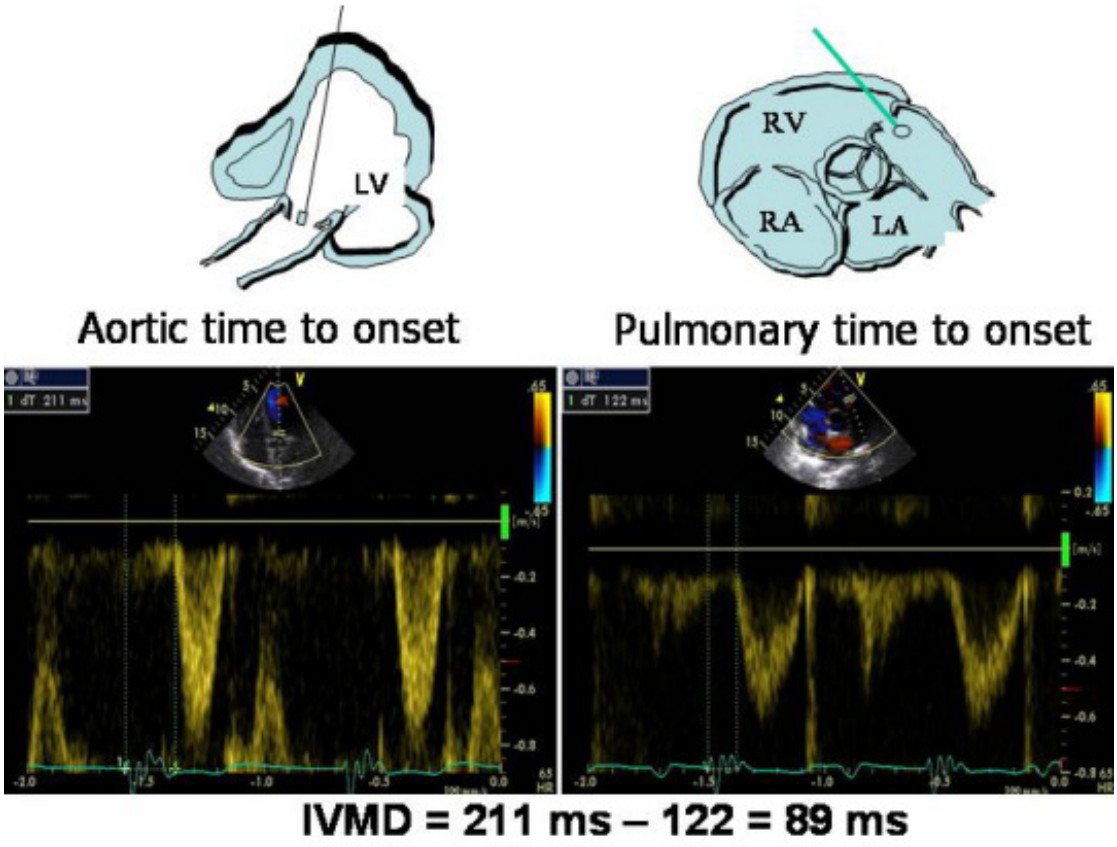


Figure 1. Measuring Aortic and pulmonary pre ejection times

Another useful parameter is a >56 ms delay between the onset of systolic motion in the basal right ventricular free wall and the most delayed basal LV segment[18,20].

The PROSPECT trial[19] a large multicenter trial was done comparing the various parameters as predictors of CRT response by Chung ES and colleagues.

They have reported only a modest role of interventricular dyssynchrony in predicting response to resynchronization therapy.

Intra ventricular dyssynchrony

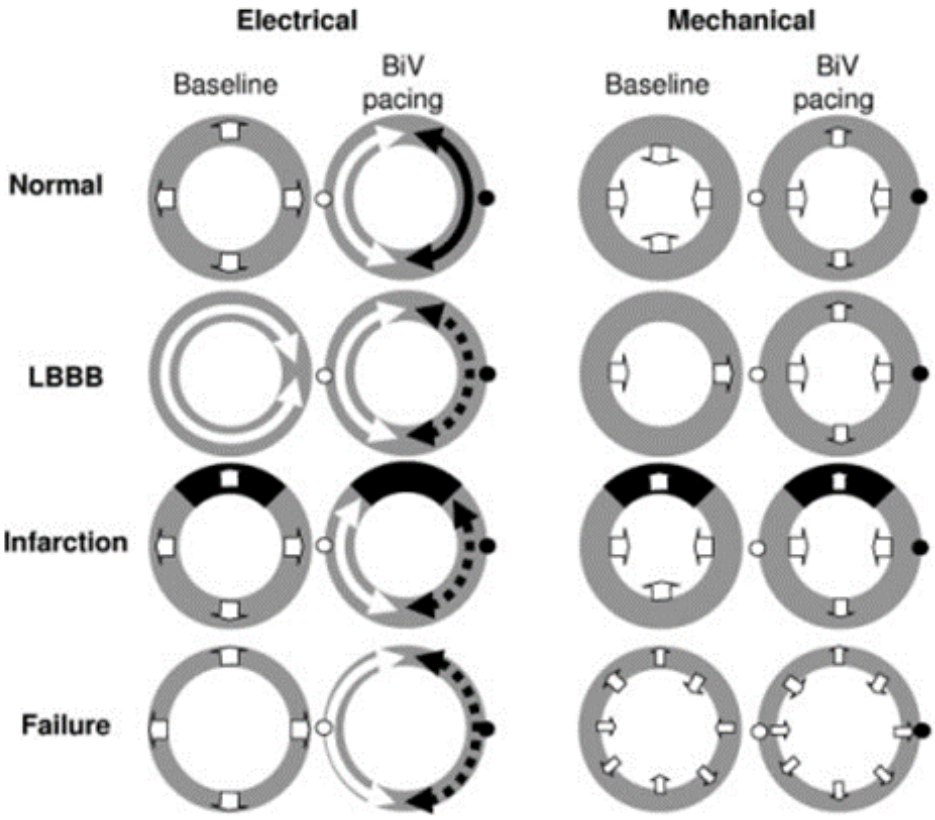


Figure 2. Temporal sequence of electrical activation and mechanical contraction in patients with LBBB, Heart failure compared with normal. The effects of biventricular pacing are shown adjacently.

The main factor associated with contractile dysfunction is altered left ventricular synchrony. CRT principally influences this factor. Hence echocardiographic Doppler assessment focuses on measurement of intraventriculardyssynchrony.

Several parameters can be assessed using standard echocardiography, tissue Doppler imaging and strain imaging. These include

By M mode and Tissue velocity imaging[18,20]

- Septal to posterior wall motion delay(SPWMD)
- Delay in Time to peak systolic velocity (Ts) between the septum and the lateral wall
- Max delay in Ts in 12 basal LV segments
- Standard deviation of Ts of 6 basal LV segments
- Asynchrony or Dyssynchrony index. Standard deviation of Ts in 12 basal and mid LV segments.

By speckle tracking and colour tissue Doppler imaging[18,20]

- Anteroseptal to posterior time to peak strain difference (radial strain)
- SD of time-to peak longitudinal strain in 12 basal and mid LV segments

BY 3D echocardiography[18,20]

- SD of time to minimum systolic volume of 16 LV segments (systolic dyssynchrony index)

3D echocardiography

Three-dimensional (3-D) echocardiography allows intra ventricular dyssynchrony to be evaluated by analyzing LVwall motion in multiple apical planes during the samecardiac cycle. It also offers better spatial resolution than a single plane.

Comparison Of Tissue Velocity Imaging And 3d Echocardiography

In a study by Sebastian A. Kleijn et al[21] published in Journal of AmericanSocietyof Echocardiography2009, tissue velocity imaging was compared with real time 3D echocardiography for the assessment of left ventricular dyssynchrony. The study was done in about 90 patients with varying ejection fractions. The control was a group of 30 healthy people. Marked differences Using one technique for the other was not clear according to the study because of the technical differences between the two modalities.

Strain imaging in assessing dyssynchrony[20]

When compared with tissue velocity imaging, strain rate imaging can differentiate active contraction and passive myocardial motion. Generally the underlying principle is unmasking post systolic shortening during diastolic myocardial relaxation time.

Few studies have compared these two modalities for assessing dyssynchrony and also for predicting CRT response.

Yu et al[22] in a study of 54 heart failure patients compared the parameters of both these methods in causing reverse remodeling of left ventricle. They concluded the standard deviation of tie to peak systolic velocity Ts SD was clinically useful in predicting LV reverse remodeling.

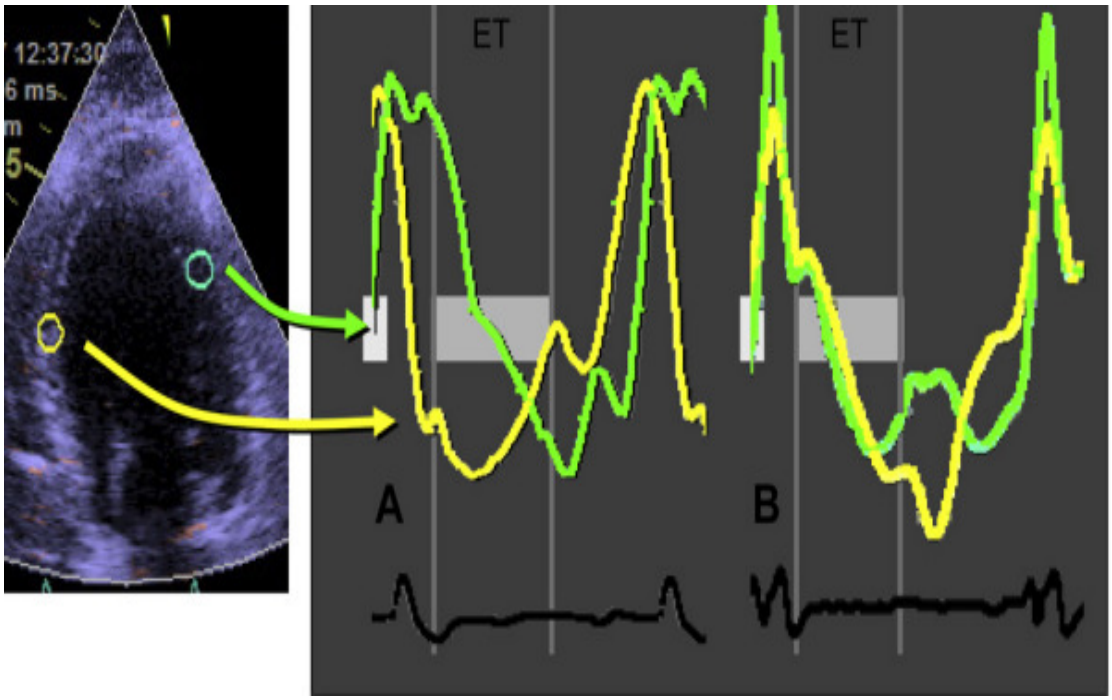


FIGURE 3. A -Longitudinal strain curves depicting different LV wall contracting dyssynchronously. B - with CRT.

Theodore P. Abraham et al[23] in a review of the role of tissue Doppler in dyssynchrony analysis concluded that septal to lateral wall delay of >65ms and Ts SD of 12 basal segments more than 33 ms were the most useful indices. The superiority of strain imaging over tissue Doppler was not conclusive in the studies according to the authors.

Antonio Vitarelli et al[24] in a review in European journal of echocardiography in 2007 have discussed the potential role of Tissue Doppler Imaging in selection of patients and optimization of CRT.

A consensus statement by Gorcsan J et al[20] published in journal of American society of echocardiography 2008 advocated the use of opposite wall by colour Doppler tissue imaging and infero lateral strain by strain imaging. The usefulness of longitudinal strain measurements have been studied in subsequent studies.

The published parameters on strain rate imaging for intraventricular dyssynchrony are as follows.

Time to peak radial strain in two basal segments (septal, posterior)	Dispersion >130 msec
Time to peak longitudinal strain in 12 basal and mid segments	Standard deviation >60 msec
Time of postsystolic contraction in 12 basal and mid segments	Sum of shortening time >760 msec

INDICES OF DYSSYNCHRONY IN TISSUE DOPPLER IMAGING

- **Septal to posterior wall motion delay (SPWMD)[18,20]**

This is assessed by M mode echocardiography. In the parasternal long axis M mode , the delay between the peak of septal contraction and peak of posterior wall contraction is measured.

Bader et al[25] in a study published in Journal of American society of echocardiography in 2004 assessed the role of septal posterior wall delays along with others. They concluded that intra LV asynchrony as assessed by these parameters in heart failure patients confers a high risk of events irrespective of QRS duration and ejection fraction.

The normal cut off values are less than 40 milliseconds. A value more than 130 milliseconds signifies dyssynchrony and a predictor of reverse remodeling after synchronization.

A poor acoustic window may limit the measurement. Altered septal motion due to pressure or volume overload of the RV and previous infarct involving septum or posterior wall also may limit the measurement.

Additionally, asynchrony in other LV walls cannot be measured. Marcus et al reported low sensitivity and specificity (25 % and 64 % respectively) for predicting CRT response.

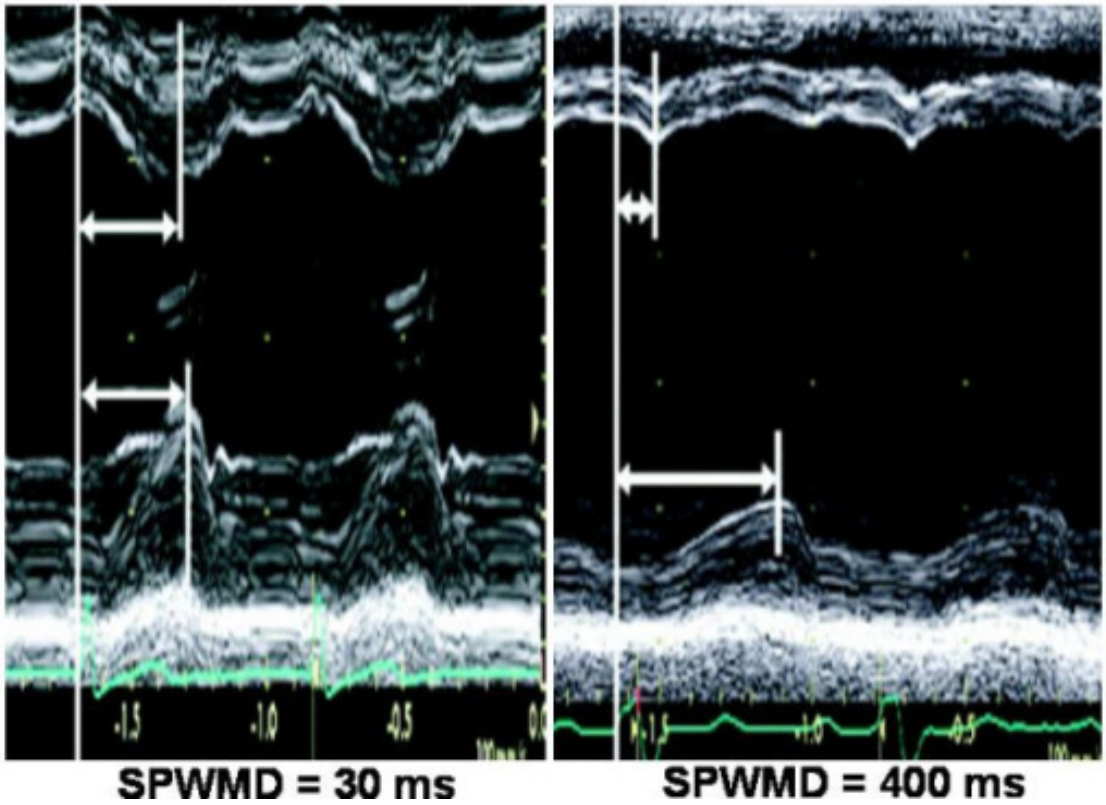


Figure 4. Measurement of septal to posterior wall delay by Mode echocardiography

- **PULSED (PW) TISSUE DOPPLER**

PWTissue Doppler has very good temporal resolution for analysing intraventricular mechanical dyssynchrony. The time to peak sustained systolic velocity is an easy measure which can be assessed by pulsed tissue Doppler imaging.

Several parameters have been advocated. Of these indices, the time interval between onset of QRS in ECG and peak systolic velocity is widely used. The measurements are made in the apical views and assess 12 LV walls[18,20]

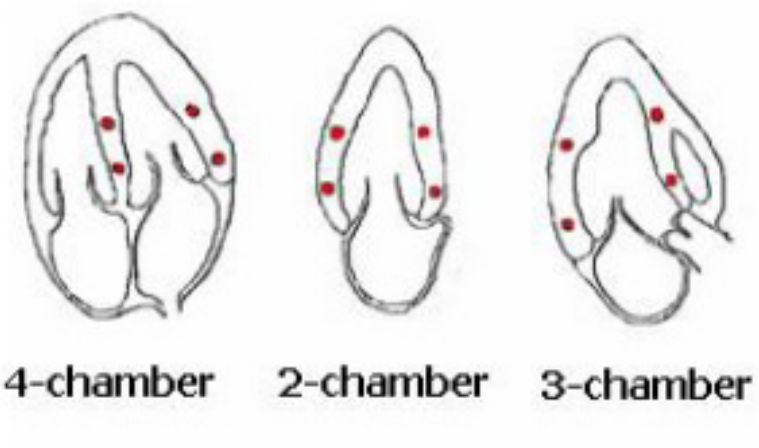


Figure 5. The 12 walls of LV where Ts is measured in pulsed Doppler

The LV segments studied in the apical view are basal anterolateral, basal septal, mid anterolateral, mid septal (in 4 chamber view) basal anteroseptal, mid anteroseptal, basal inferolateral, mid inferolateral (in

3 chamber view) basal anterior, mid anterior, basal inferior, mid inferior (in 2 chamber view)

Typically Intra ventricular asynchrony has been defined as a difference of > 65 ms of time to peak (Ts) between LV segments.

Bader H et al[25] reported a sensitivity of 80% and specificity of 92% to predict clinical and pathological improvement after synchronization.

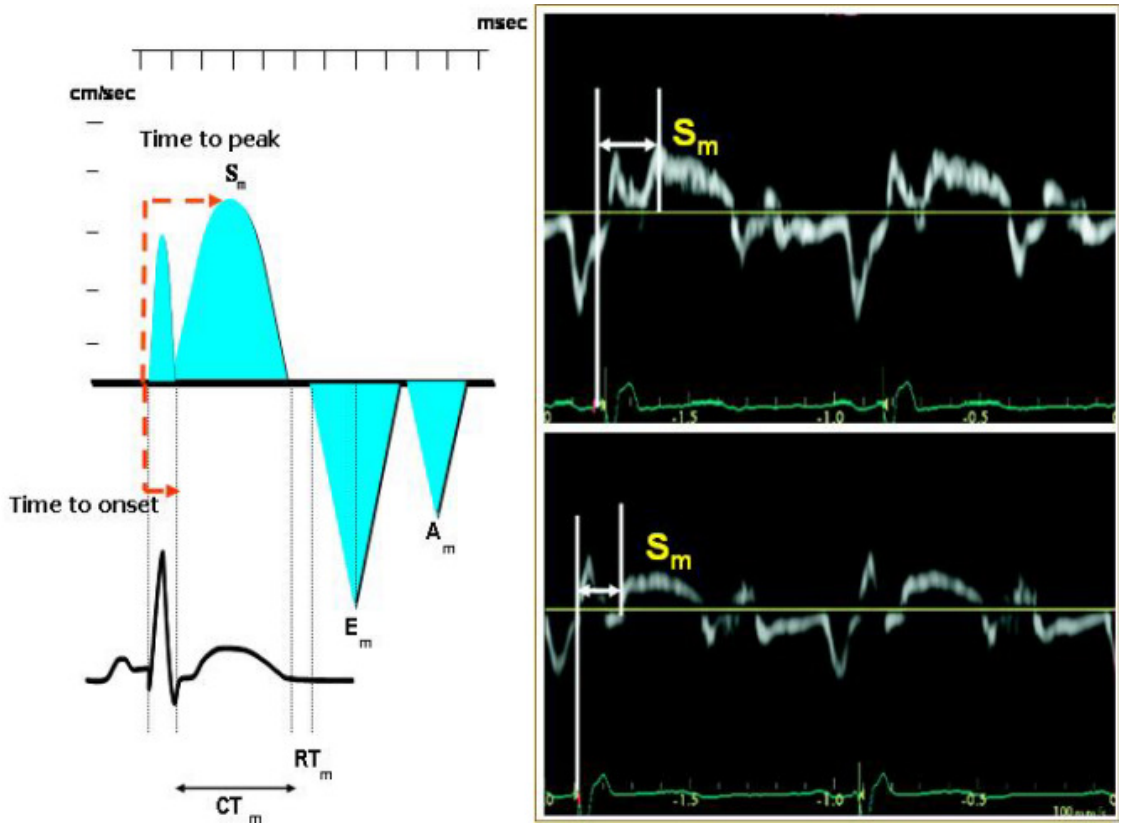


Figure 6.Method of measuring time to peak systolic velocity (Ts)

CT – contraction time, RTm – Myocardial relaxation time, Sm –myocardial systolic velocity, Em – early diastolic velocity.

Dyssynchrony index

Dyssynchrony index calculated by the standard deviation of the average values of time to peak systolic velocity - Ts SD of the 12 LV segments more than 33 ms is considered as dyssynchrony.

Yu et al[26] in a study in 2003 found that the dyssynchrony index (DI) more than 32.6 ms predicted with 100 % sensitivity and specificity improvement in LV remodeling after CRT.

The summary of various studies on the echocardiographic techniques in assessing dyssynchrony , useful parameters and reference values is given below[26,27,28].

Technique	Parameter	Authors	Cut-off point
M-mode	SPWMD	Pitzalis et al, J Am Coll Cardiol 2002	> 130 ms
M-mode and PW Doppler	LWPSD	Sassone et al, Am J Cardiol 2007	> 1
PW Tissue Doppler	Diff. of T_s between LV segments	Bax JJ et al, J Am Coll Cardiol 2004	> 65 ms
TVI	T_s-SD	Yu et al, Am J Cardiol 2003	> 32.6 ms
TSI	T_s-SD	Yu et al, J Am Coll Cardiol 2005	> 34.4 ms
SRI	TPS-SD	Mele et al, Eur Heart J 2006	> 60 ms
SRI	ExcT	Porciani MC et al, Eur Heart J 2006	> 760 ms
2D radial strain	Time diff. in peak septal wall-to-posterior wall strain	Suffoletto et al, Circulation 2006	≥ 130 ms

Figure 7. Table of various studies of the different echocardiographic techniques and indices.

MECHANICAL DYSSYNCHRONY IN HEART FAILURE PATIENTS WITH NARROW QRS

Several studies have demonstrated that mechanical dyssynchrony occurs in heart failure patients irrespective of the QRS duration.

Stefano Ghio et al[3] in a study showed that interventricular dyssynchrony defined by interventricular mechanical delay greater than 40 ms was present in 12.5 % of heart failure patients and intraventricular dyssynchrony in 29.5 % of the patients.

Zahra Emkanjoo et al[9] in a study published in 2007, showed the occurrence of interventricular dyssynchrony in 42.5 % of heart patients with normal QRS

duration compared to patients with wide QRS. The frequency of intraventricular dyssynchrony also was higher in the normal QRS group 45% compared to 23% in patients with wide QRS.

Smita Mehta and Samuel J Asirvatham in an article published in 2012[29] propose that the electromechanical coupling seen in some heart failure patients with normal QRS may be due to small areas of myocardial infarction or fibrosis sparing conducting system.

TRIALS OF CRT BASED ON QRS DURATION

The MADIT CRT[30] and REVERSE[31] trials showed that in patients with wide QRS complexes and severe LV dysfunction CRT showed benefit.

The Cardiac Resynchronization in Heart Failure (CARE-HF) trial[32] and several single center studies have documented that echo based mechanical dyssynchrony parameters (most of which are based on echocardiographic measures) have greater accuracy than QRS width to predict outcome improvement after CRT and long-term outcome. But in PROSPECT (Predictors of Response to

CRT) study[19], these results were questioned. No single LV mechanical dyssynchrony parameter could accurately predict response to CRT.

The RETHINQ study[33] in 2007, failed to show any benefit in heart failure patients with narrow QRS and dyssynchrony in echocardiography.

Another trial which studied CRT in narrow QRS patients, the NARROW CRT trial[34] reported in 2013 was based on a small randomized sample of heart failure patients. The group had echo criteria for dyssynchrony. The study concluded that CRT improved clinical status in this group of patients with mild to moderate symptoms.

The most recent trial addressing this issue was the ECHO – CRT trial[11]. This was a randomized multicenter trial involving Patients in NYHA Class III or IV heart failure with LVEF <= 35%, diastolic LV dimension greater than 5.5cm, QRS duration < 130 milliseconds and dyssynchrony assessed by tissue Doppler and speckle tracking. All eligible patients underwent biventricular ICD with randomization to CRT on versus CRT off. The study was terminated prematurely. The CRT group had higher death which was statistically significant.

Currently guidelines do not recommend CRT for heart failure patients with narrow QRS.

MATERIALS AND METHODS

All patients with heart failure (ejection fraction <35%) with normal QRS duration attending outpatient clinic or admitted in cardiology wards were included in the study. Patients with preexisting LBBB, RBBB and paced individuals were excluded from the study.

Inclusion criteria

All heart failure patients with ejection fraction less than 35% and narrow QRS (less than 120 milliseconds) with duration of symptoms 6 months or more irrespective of the etiology attending outpatient department or admitted in wards were included in the study.

Exclusion criteria

1. Patients with pre existing LBBB OR RBBB
2. Paced individuals
3. Patients with wide QRS
4. Patients with duration of symptoms less than 6 months
5. Patients with NYHA class IV

METHODOLOGY

After obtaining informed consent , thirty consecutive heart failure patients who fulfilled the inclusion criteria were included in the study.

The study was conducted at the Department of Cardiology, RajivGandhi General Hospital,Chennai over a period of 6 months.

Clinical details including the duration of symptoms, NYHA class ,presence or absence of Coronary artery disease, diabetes, hypertension, chronic kidney disease, valvular heart disease, toxins were obtained from the patients. A 12 lead ECG was recorded and the duration of QRS noted.

All patients underwent detailed Echocardiographic evaluation. Echocardiogram was performed using PHILIPS HD7XE machine.

All the patients underwent detailed echocardiographic study. Echocardiogram was done using Philips HD7XE Echocardiographic machine. Echocardiographic assessment of LV end diastolic and end systolic volumes, ejection fraction, Tricuspid annular planar systolic velocity, aortic and pulmonary pre ejection times, septal to posterior wall delay, time to peak systolic velocity (Ts)of 12 LV segments LV was done and assessed for dyssynchrony.

STATISTICAL ANALYSIS

The data were entered and analyzed in SPSS Statistics Version 17.0.1. Clinical characteristics of the respondents were analyzed as frequencies, proportions, means and standard deviations. Similarly the echocardiographic measurements were also analyzed. The bivariate correlations between the indicators of intra-ventricular dyssynchrony such as Ts-SD, Ts-Diff and SPWMD were assessed using simple scatter plots and Pearson's correlation coefficient. The relationships between the interventricular dyssynchrony indicated by the Inter Ventricular Mechanical Delay (IVMD) and the duration of the QRS in ECG were studied using scatter plot and simple linear regression. Similarly relationships of indicators of intra ventricular dyssynchrony indicators such as Ts-SD, Ts-Diff and SPWMD with the QRS duration were also studied. The association between IVMD and Ts-SD were studied using simple scatter plot and linear regression. It was also studied using Chi Square test after categorizing the IVMD based on a cut off of 40 ms and Ts-SD on a cut off of 33.4 ms. Scatter plots with non-significant linear relationships were smoothed using the Lowess method.

RESULTS AND DATA ANALYSIS

Clinical characteristics of the study population.

30 patients fulfilling the inclusion criteria were included in the study.

The average age of the study population was 45.27 years. The majority of the study participants were male comprising 86.7% (n=26).

All the study group had symptomatic heart failure. 56.7 % (n=17) had NYHA class III symptoms and 43.4 %(n=13) had class II symptoms. All the patients were on treatment.

All the patients had duration of symptoms more than 6 months. The mean duration of symptoms was 11.03 months (SD 4.54).

Narrow QRS duration (120 milliseconds or less) was the primary inclusion criteria for the study population. The mean width of QRS duration in the study group was 95.67 (SD 10.24) ms.

Among the study group , history of coronary artery disease was present in 30 % (n=9). 20 % (n=6) of the study population had chronic kidney disease.13.3 % (n=4) had valvular heart disease with heart failure. Two patients had severe aortic stenosis and aortic regurgitation and two patients had severe mitral

regurgitation and severe aortic regurgitation. 36.7% of the group (n=11) comprised of non ischemic dilated cardiomyopathy. Diabetes mellitus (20%) and hypertension (26.7%) were additional risk factors for heart failure present in the study population primarily associated with patients with coronary artery disease and chronic kidney disease.

TABLE .1 Clinical Characteristics of study participants

Characteristic	
Age	45.27 (SD 13.06) years
Gender (Male)	26 (86.7%)
NYHA Class	
Class II	13 (43.3%)
Class III	17 (56.7%)
Mean duration of symptoms	11.03 (SD 4.54) months
Reason for Heart Failure	
• **Diabetes**	6 (20%)
• **Hypertension**	8 (26.7%)
• **Coronary Heart Disease**	9 (30%)
• **Chronic Kidney Disease**	6 (20%)
• **Dilated Cardiomyopathy**	11 (36.7%)
• **Valvular Heart Disease**	4 (13.3%)
Mean Width of QRS in ECG	95.67 (SD 10.24) ms

Echocardiographic parameters

All the patients in the study group had ejection fraction of 35 % or less. 30.37 (SD 4.38) % was the average ejection fraction measured in the study group.

The mean end diastolic LV volume in the study population was 151.80 (SD 19.22) ml and the end systolic volumewas105.87 (SD 20) ml.

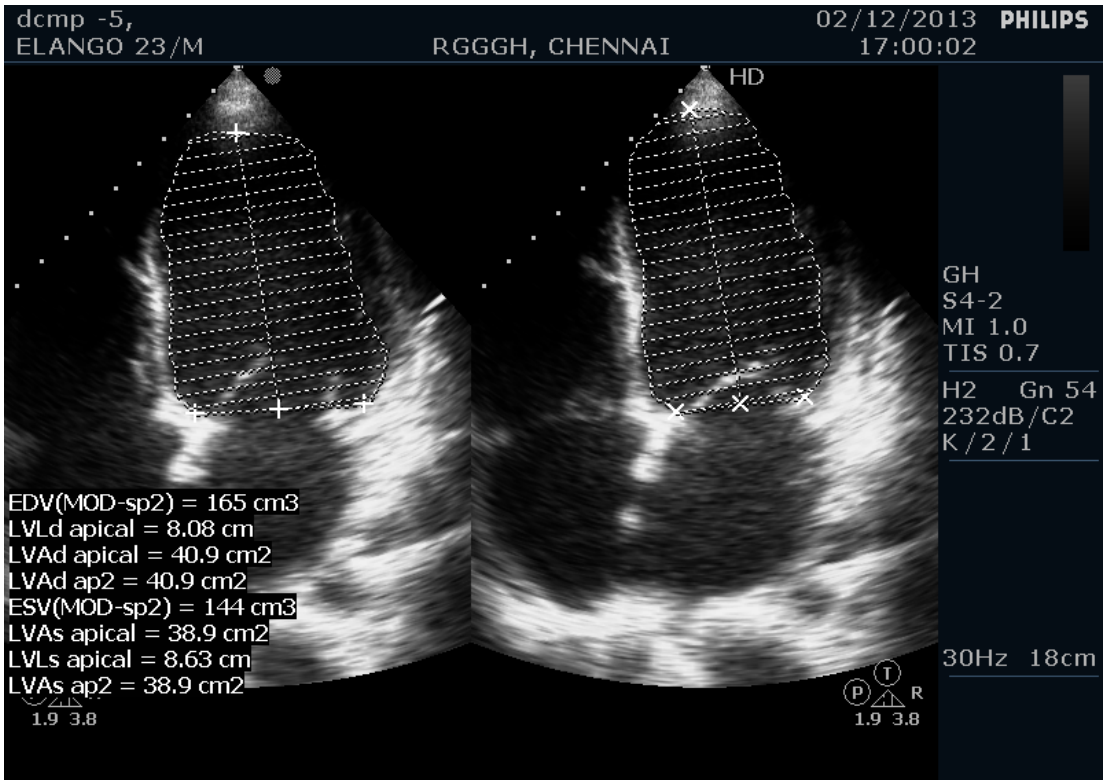


Figure 8. Assessment of ejection fraction by modified Simpson's method.

Taking a cut off value of 16 for the Tricuspid annular plane systolic excursion , Right ventricular dysfunction was present along with left ventricular dysfunction in 6 patients (20%).The average TAPSE of the study group was 17.43 (SD 2.69).

INTERVENTRICULAR ELECTROMECHANICAL DELAY

The aortic pre ejection time measured in the group ranged from 76 ms to 128 ms mean being 105.33 (SD 16.35) ms. The pulmonary pre ejection time ranged from 70 ms to 118 ms, the average value being 87.23 (SD 11.24) ms.

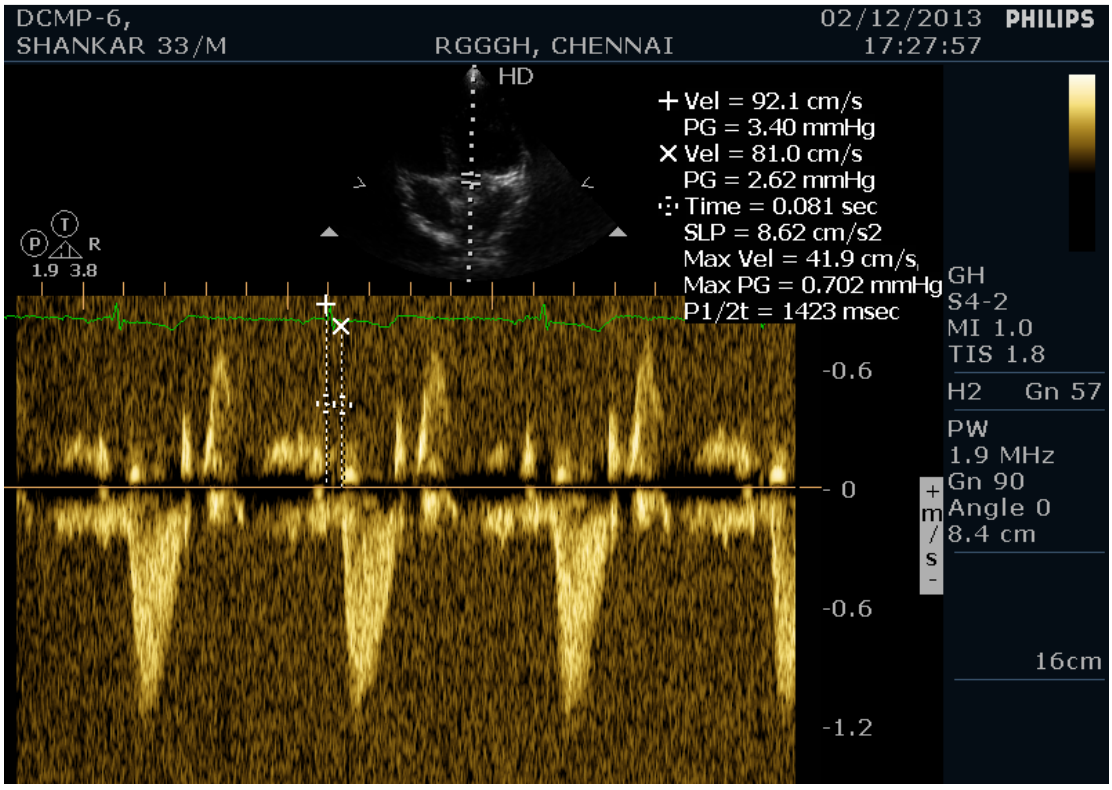


Figure 9. Measurement of aortic pre ejection time.

A difference of more than 40 millisec between the Aortic pre ejection time and pulmonary pre ejection time was taken as the cut off . Based on that interventricular dyssynchrony was present in 20% of the patients (n=6). The mean time difference was 23.7 (SD 13.9) ms.

INTRAVENTRICULAR ELECTROMECHANICAL DYSSYNCHRONY

Septal to posterior wall delay was measured in M mode echocardiography parasternal long axis. The values ranged from 58 ms to 134 ms , average being 90.73 (SD 27) ms.A value of more than 130 ms was taken as significant and 16.7 % (n=5) of the study group had a value of more than 130 ms.

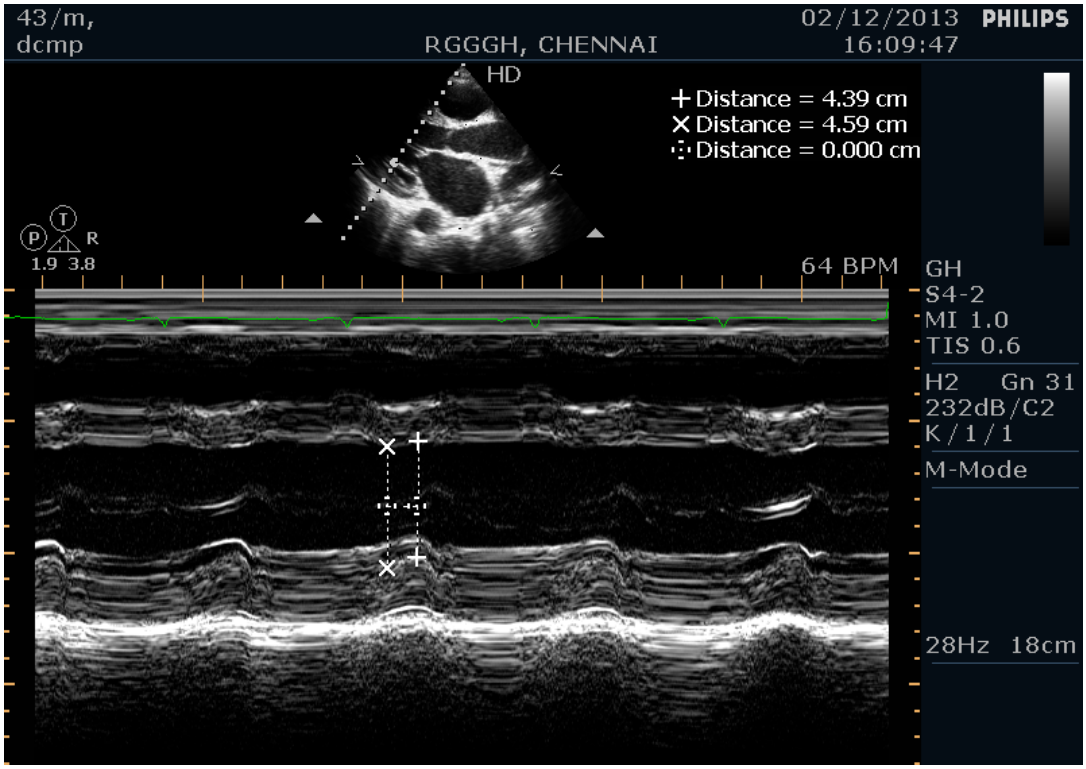


Figure 10. Measurement of septal to posterior wall delay

Time to peak systolic velocity (Ts)

The time to maximal systolic velocity was measured in 12 LV segments using Tissue Doppler imaging. From the values Standard deviation of the values for each patient was arrived at, Ts –SD. The Ts-SD of the study group had a mean value of21.12 (SD 9.71) ms.

The maximal difference between Ts of any two segments Ts-Diff had a mean of 67.97 (SD 32.82) ms. Based on a cut off value of TS-diff more than 100 ms , 23.3 % (n=7) of the study population had intraventricular dyssynchrony.

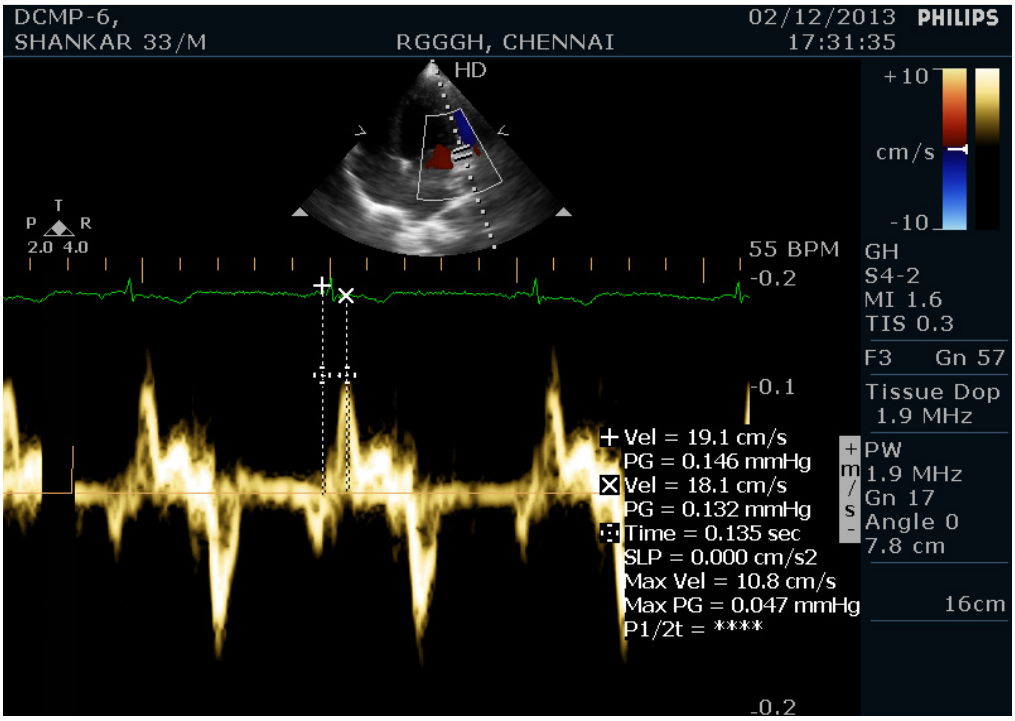


Figure 11. Measurement of Ts of basal anterolateral wall in apical 4 chamber view using tissue Doppler imaging.

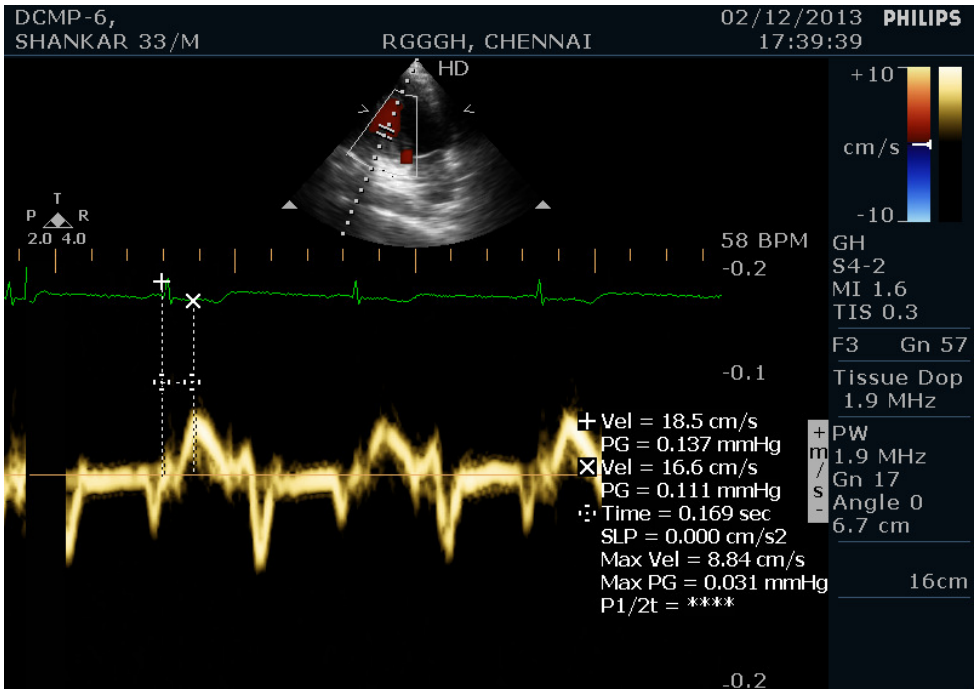


Figure 12. Measurement of Ts of mid inferior wall in apical 2 chamber view using tissue Doppler imaging.

Dyssynchrony index

The cutoff value for Ts-SD of the 12 LV segments (Dyssynchrony index) was taken as >33.4 ms and accordingly intraventricular dyssynchrony was present in 23.3% (n=7).

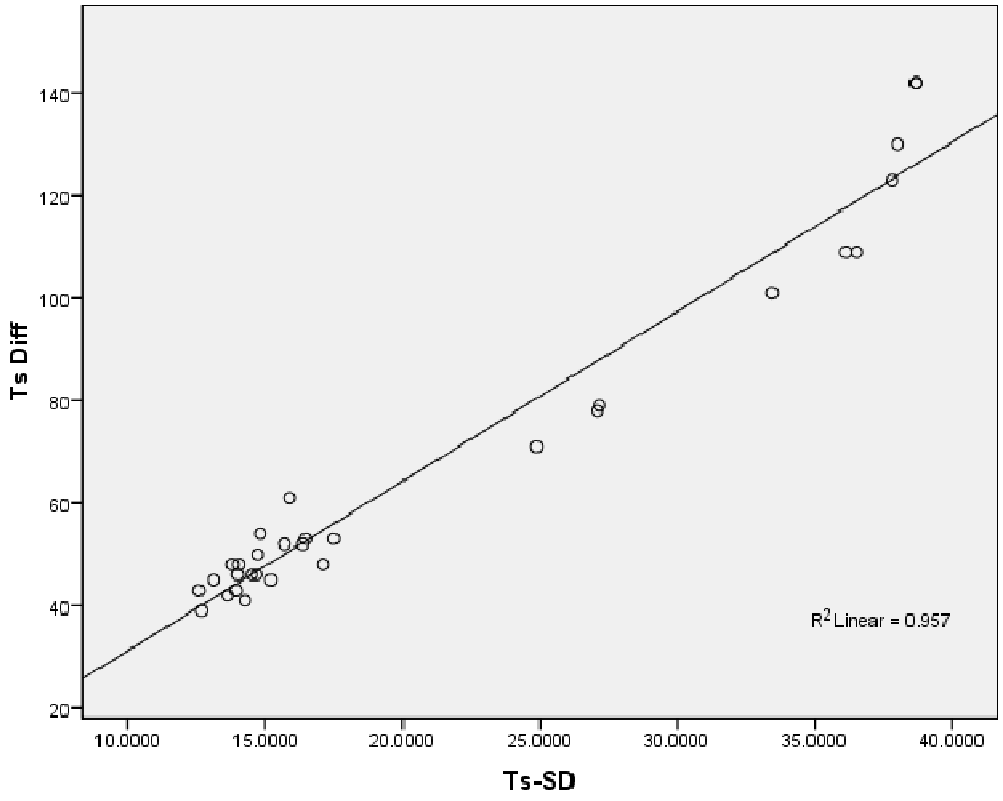
TABLE 2 .Echocardiographic parameters

Variable	Values
End Diastolic LV Volume	151.80 (SD 19.22) ml
End Systolic LV Volume	105.87 (SD 20) ml
LV Ejection Fraction	30.37 (SD 4.38) %
Tricuspid Annular Plane Systolic Excursion	17.43 (SD 2.69)
Aortic Pre-Ejection Time	105.33 (SD 16.35) ms
Pulmonary Pre-Ejection Time	87.23 (SD 11.24) ms
Septal to Posterior Wall Motion Delay	90.73 (SD 27) ms
SPWMD (≥ 130 ms)	5 (16.7%)
Inter Ventricular Dyssynchrony	23.7 (SD 13.9) ms
Inter Ventricular Dyssynchrony (≥40 ms)	6 (20%)
Ts-SD	21.12 (SD 9.71) ms
Ts-SD (≥33.4 ms)	7 (23.3%)
Ts-Diff	67.97 (SD 32.82) ms
Ts-Diff (≥100 ms)	7 (23.3%)

Correlation between the intra-ventricular Dyssynchrony indicators

The bivariate correlations between the various intraventricular dyssynchrony indicators Ts-SD, Ts-Diff and SPWMD such as were assessed. This was done using simple scatter plots and Pearson's correlation coefficient.

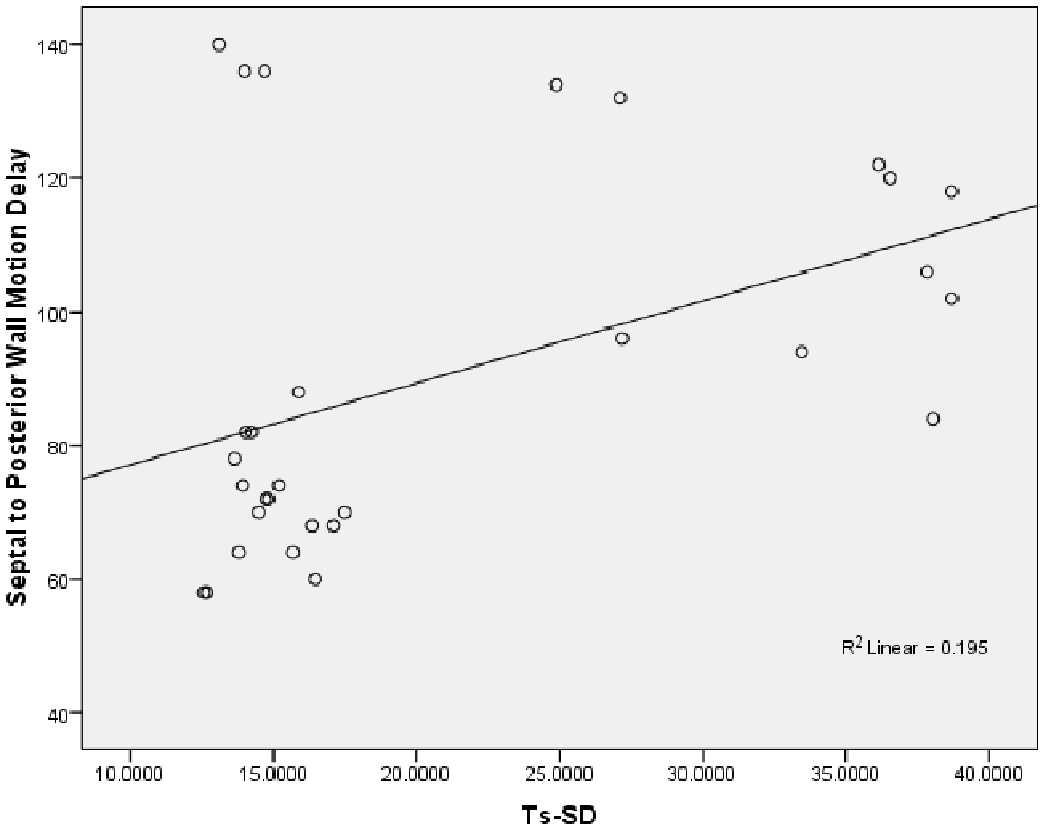
Ts-SD vs Ts-Diff



Pearson's Correlation Coefficient : 0.978 ($p<0.001$)

Simple scatter plot showed significant correlation between the indices, Ts – SD and Ts diff.(Pearson's Correlation Coefficient : 0.978 ($p<0.001$))

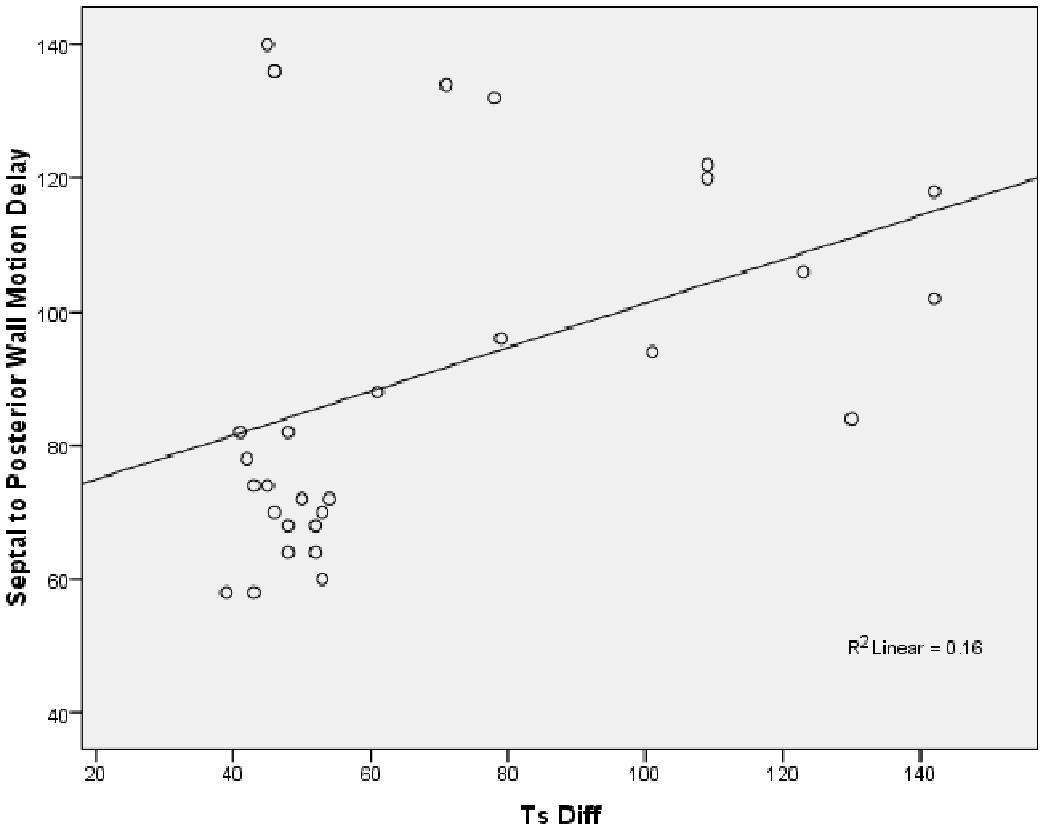
Ts-SD versus SPWMD



Pearson's Correlation Coefficient : 0.441 (p=0.015)

The correlation between septal to posterior wall delay and Ts-SD was also significant but less compared to that between Ts-SD and Ts diff.

Ts-Diff vs SPWMD

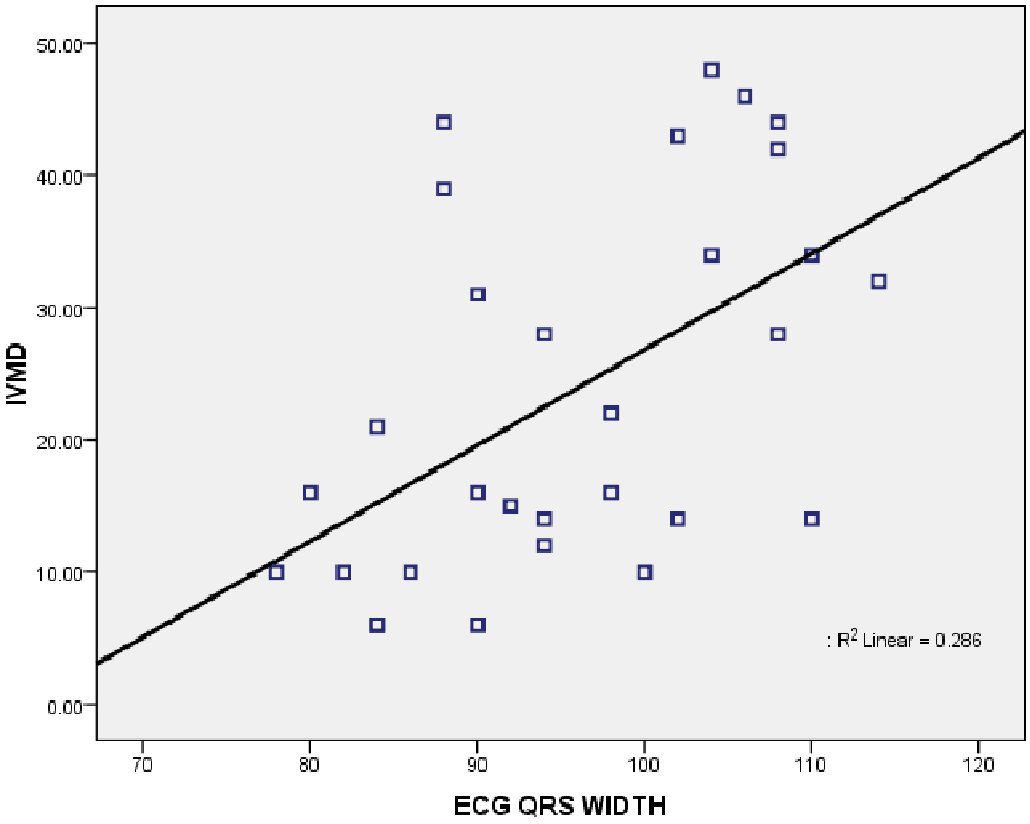


Pearsons Correlation Coefficient: 0.4 (p = 0.028)

Simple scatter plot of correlation between SPWMD and Tsdiff was also less significant statistically.

Relation between Inter Ventricular Dyssynchrony and QRS Duration

Relation between Inter Ventricular Dyssynchrony and QRS Duration was also studied using scatter plots and simple linear regression.



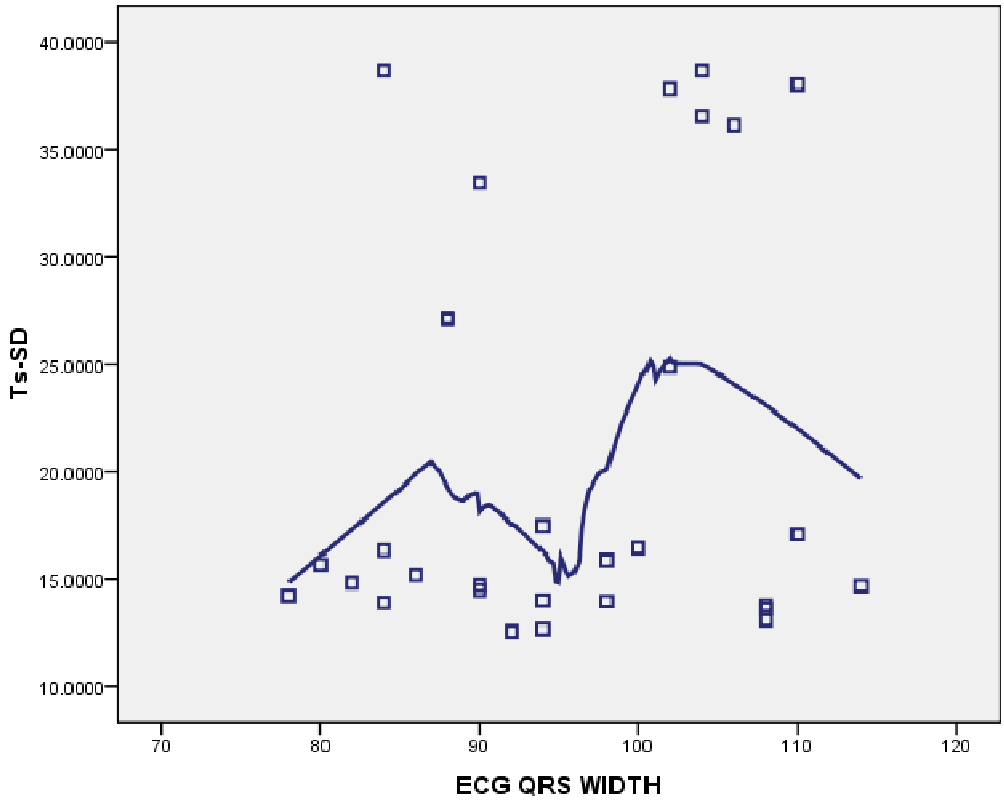
The scatter plot showed a statistically significant linear fit of the observations. The R^2 is 0.286 which indicates a low precision of the linear fit. This is probably due to the small sample size. Linear regression indicates a relationship

between IVMD and ECG QRS duration (β = 0.394, 95% CI 0.153 - 0.635, p = 0.002).

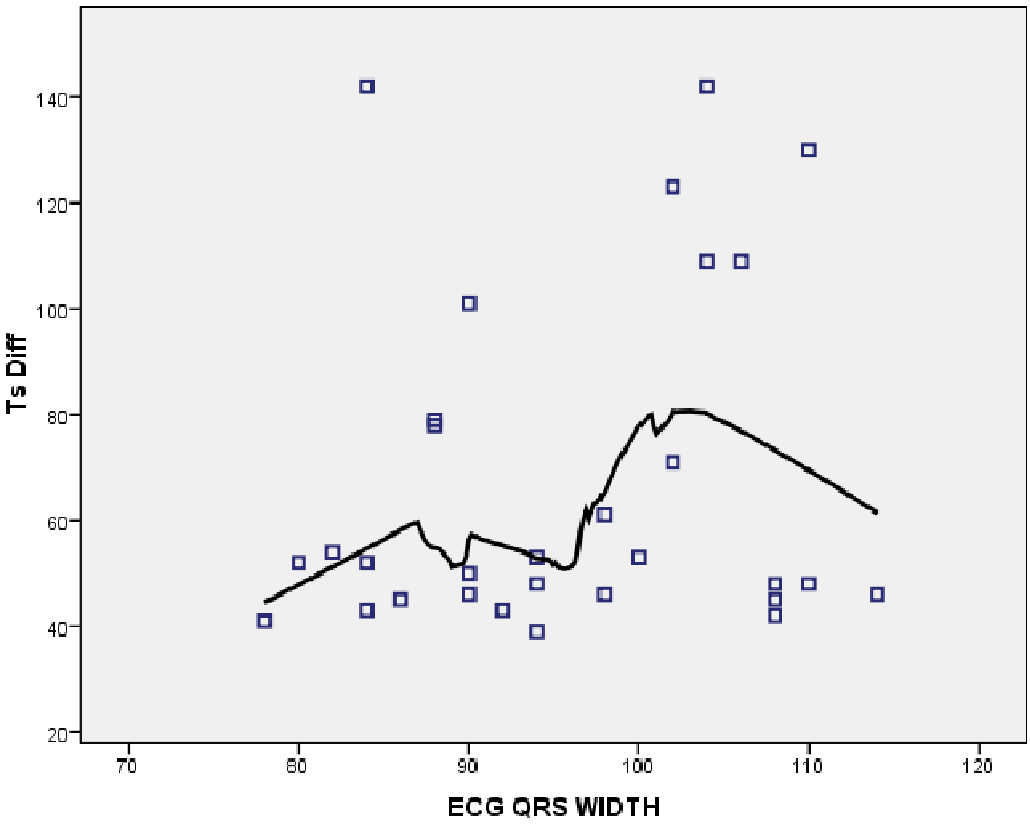
Intra ventricular dyssynchrony indicators with the QRS duration

Relationships of indicators of intra ventricular dyssynchrony indicators such as Ts-SD, Ts-Diff and SPWMD with the QRS duration were also studied using scatter plots and simple linear regression.

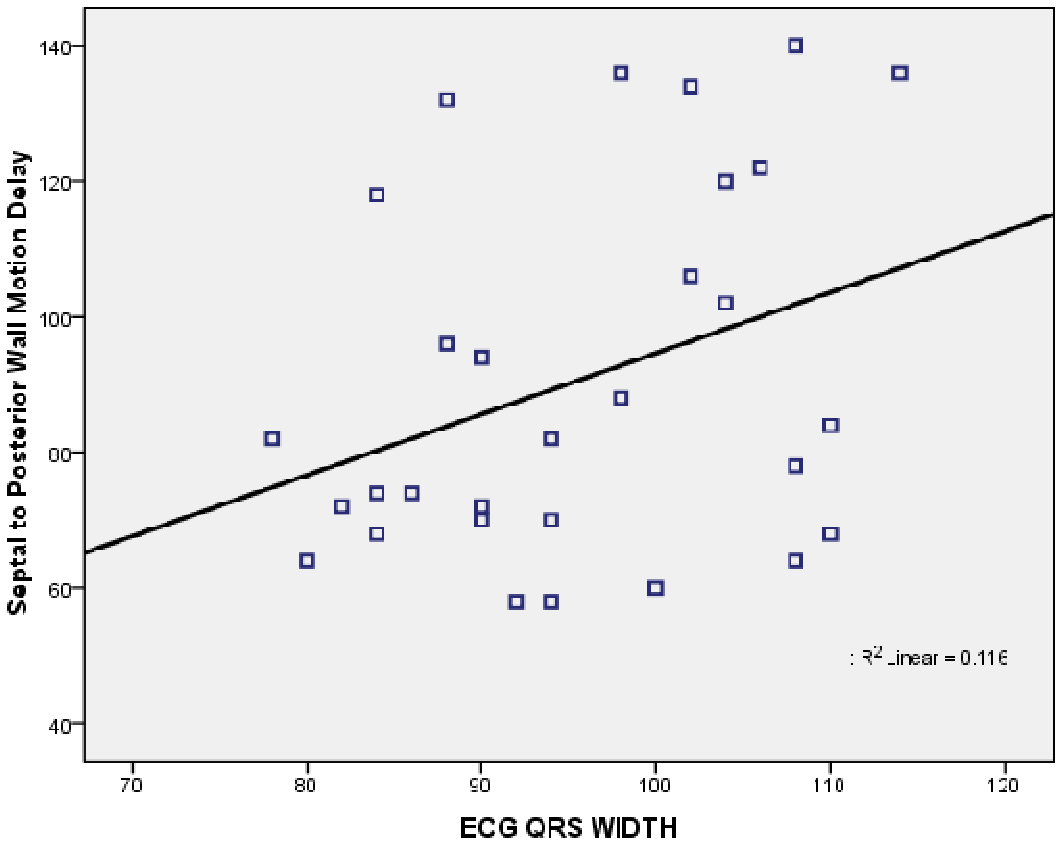
1. Relation between Intra Ventricular Dyssynchrony and QRS duration



The scatter plot did not show a linear fit. The curve was smoothed using Lowess method. Linear regression does not indicate any association between Ts-SD and QRD width in ECG ($\beta = 0.203$, 95% CI -0.197 – 0.604, $p = 0.308$)

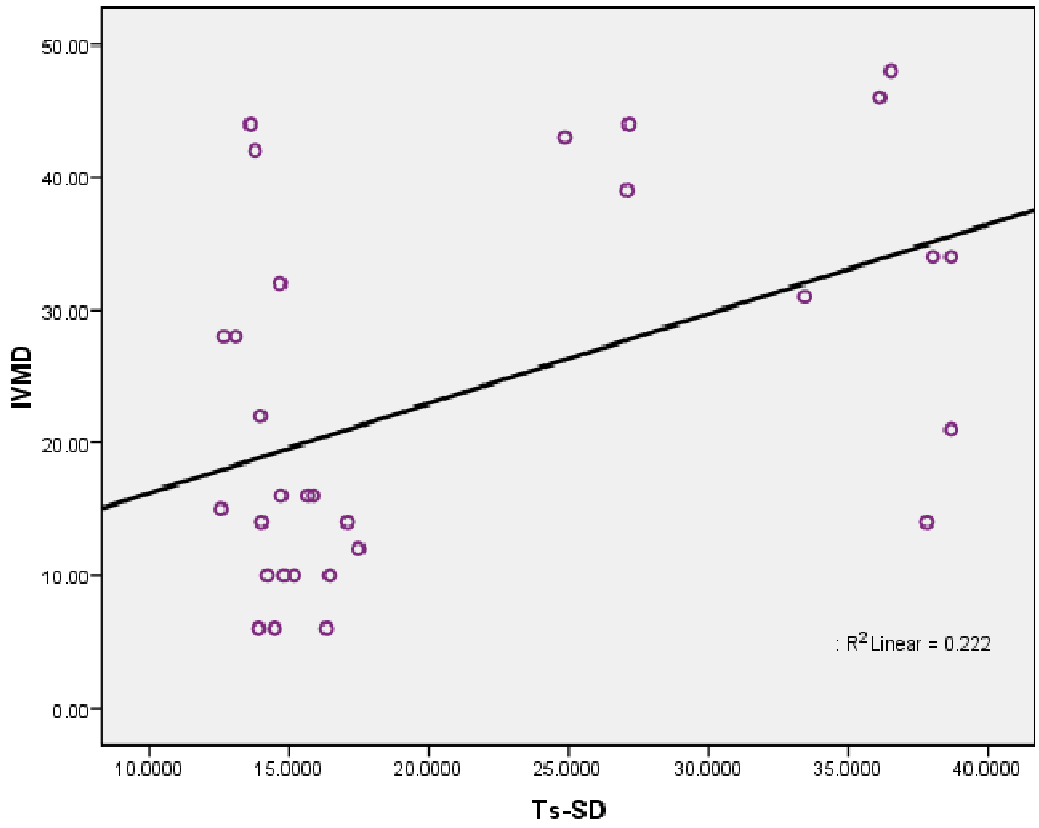


The scatter plot did not show a linear fit. The curve was smoothed using Lowess method. Linear regression did not indicate any association between Ts-Diff and QRS width in ECG ($\beta = 0.058$, 95% CI -0.061 – 0.176, $p = 0.329$)



Though there seems to be a linear trend in the scatter plot this was not statistically significant. The R^2 value is 0.116 which is very low. Linear regression did not indicate any association between SPWMD and QRS width in ECG (β = 0.129, 95% CI -0.009 – 0.267, p = 0.065). But since the lower bound of the CI is very small and close to 0, it is likely that there is a chance of type 2 error. Therefore there is a chance that this association may become statistically significant if the sample size is increased.

2. *Association between Inter Ventricular Mechanical Delay and total Asynchrony Index*



The scatter plot showed a statistically significant linear fit of the observations. The R^2 was 0.222 which indicates a low precision of the linear fit probably due to the small sample size. Linear regression indicates a relationship between IVMD and Ts-SD ($\beta = 0.329$, 95% CI 0.091 - 0.568, $p = 0.009$).

Association between Inter Ventricular Mechanical Delay (IVMD) and Total Asynchrony Index

	Ts –SD ≥ 33.4 ms	**Ts – SD < 33.4 ms**
IVMD ≥ 40 ms	2	4
IVMD < 40 ms	5	19

Pearson's Chi Square: 0.419 p value: 0.603

There seems to be low association between the IVMD and Ts-SD in the study patients.

DISCUSSION

This study was undertaken to assess the frequency of electromechanical dyssynchrony in heart failure patients with a QRS width of 120 ms or less. Also the relationship between the individual indices to one another was also studied.

The frequency of intraventricular dyssynchrony in this study was 23.3% based on Ts SD and Ts diff. Several studies have documented the prevalence of dyssynchrony to be ranging from 30% -50% in heart failure patients with narrow QRS.

Stefano Ghio et al[3] in a study of 158 heart failure patients with normal and wide QRS showed that 29.5% patients with normal QRS had intraventricular dyssynchrony . In the group with wide QRS (120ms - 150 ms) the frequency was 57.1 % and in the group with very wide QRS (>150 ms) the prevalence was 71%.

Yu CM et[26] al in prospective a study of the presence of LV systolic and diastolic dyssynchrony in heart failure patients with normal QRS assessed by tissue Doppler imaging showed that 51% had systolic asynchrony and 46 % had diastolic asynchrony.

Zahra Emkanjoo et al[9] in a study in 2007, showed the occurrence of intraventricular dyssynchrony in a higher in the normal QRS group 45% compared to 23% in patients with wide QRS.

The occurrence of intraventricular dyssynchrony in the present study was 16.7 % based on septal posterior wall motion delay. Several studies have disputed the predictive value of this index in assessing the response to synchronization. Also it is affected by previous infarcts in the septal or posterior walls, right ventricular pressure or volume overload.

The occurrence of interventricular dyssynchrony in the study group was 20 % based on the cut off value of >40 ms . Interventricular dyssynchrony based on this index has been reported in several studies in patients with normal QRS duration.

In a study byZahra Emkanjoo et al[9] inter ventricular dyssynchrony was present in 26.8% of normal QRS group compared to 42.5% in patients with wide QRS .

In a study byStefano Ghio et al[3]interventricular dyssynchrony (defined by the presence of an interventricular mechanical delay greater than 40 ms) was found in 12.5% of patients with normal QRS width.

The correlations between the various intraventricular dyssynchrony indicators Ts-SD, Ts-Diff and SPWMD were assessed in the study. Among the indices the correlation between Ts –SD and Ts diff was greater compared to the correlation between SPWD and the other two indices. Septal to posterior wall delay is affected by factors other than electromechanical uncoupling as the cause of dyssynchrony. Many studies which measured intraventricular dyssynchrony used the indices of Ts SD and Ts diff than SPWD.

The dyssynchrony index and maximal difference in systolic velocities measure longitudinal dyssynchrony in a complete manner. Offline analysis can also be made.

The study by Notabartolo et al[35] showed that the peak velocity difference is an important index of dyssynchrony and also showed its usefulness in predicting CRT response.

The study by Yu CM et al[26] regarding utility of tissue Doppler velocity and strain dyssynchrony in assessing outcomes after cardiac resynchronization therapy showed the usefulness of the dyssynchrony index in this regard.

In the study group relationships of indicators such as Ts-SD, Ts-Diff and SPWMD with the QRS duration did not show any correlation. This

issue has been addressed in several studies which have questioned the width of QRS as a marker of Dyssynchrony. The reason for this could be different mechanisms operating for the mechanical delay such as abnormal loading conditions. Other reasons advocated for this are probable small areas of myocardial infarction or fibrosis sparing conducting system as proposed by Smita Mehta and Samuel J Asirvatham[29] .

In the study population there seems to be low association between the IVMD and dyssynchrony index. The mechanisms behind Interventricular dyssynchrony and regional altered LV contraction are different . There is no association between them as seen in several studies assessing dyssynchrony.

Limitations of the study

Though the sensitivity and specificity of Tissue Doppler imaging in assessing dyssynchrony has been very well validated, newer modalities like strain imaging would have added to the assessment of asynchrony.

CONCLUSION

1. Intra and interventricular dyssynchrony occur in a significant proportion of heart failure patients with a QRS duration of 120 ms or less. The prevalence of intra ventricular electromechanical dyssynchrony was 23% and interventricular dyssynchrony 16 %

2. Among the indices of intraventricular dyssynchrony, The dyssynchrony index(Ts-SD) and peak velocity difference
   (Ts diff) show good inter parameter correlation compared to septal posterior wall motion delay SPWMD.

3. There is no association between the QRS duration and the dyssynchrony parameters in the study.

4. There is no association between interventricular dyssynchrony and intraventricular dyssynchrony.

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ACRONYMS

RV	-	Right Ventricle
LV	-	Left Ventricle
TDI	-	Tissue Doppler imaging
SRI	-	Strain rate imaging
3DRTE	-	Three dimensional real time echocardiography
LWPSD	-	Lateral wall post-systolic displacement
PW	-	pulse wave
SPWMD	-	Septal-to-posterior wall motion delay
TSI	-	Tissue synchronization imaging
TVI	-	Tissue velocity imaging
Ts-SD	-	Standard deviation of time to peak Sm
Ts diff	-	maximal difference between peak systolic velocity
TPS-SD	-	Standard deviation of time to peak strain
TAPSE	-	Tricuspid Annular Plane Systolic Excursion
EF	-	Ejection Fraction
CRT	-	Cardiac resynchronization therapy.

PROFORMA

ECHOCARDIOGRAPHIC ASSESSMENT OF INTER AND INTRAVENTRICULAR DYSSYNCHRONY IN HEART FAILURE PATIENTS WITH NORMAL QRS DURATION

Name :Date:

Age/Sex: OP/IP No:

Occupation:

Income:

Address:

Phone number:

CLINICAL CHARACTERISTICS

DURATION OF SYMPTOMS:

NYHA CLASS :

CAD / DIABETES / HYPERTENSION / CHRONIC KIDNEY DISEASE/ VALVULAR HEART DISEASE/ DILATED CARDIOYOPATHY

SMOKING / ALCOHOL INTAKE

ECG QRS WIDTH :

OTHER FINDINGS :

ECHOCARDIOGRAPHIC PARAMETERS

End-diastolic LVvolume :End-systolic LVvolume :

LVEF (%) :

MITRAL REGURGITATION (JET AREA METHOD) :

LV DIASTOLIC DYSFUNCTION :

MEAN PULMONARY ARTERY PRESSURE :

TAPSE : TRICUSPID REGURGITATION :

Intraventricular electromechanical delay

Aortic pre-ejectioninterval (ms) :

Pulmonicpre-ejectioninterval (ms):

Interventricularelectromechanicaldelay (ms)

T_S (Time to peak myocardial systolic velocity) (ms)

APICAL FOUR CHAMBER VIEW BASAL ANTEROLATERAL :

BASAL SEPTAL :

MID ANTERO LATERAL ;

MID SEPTAL :

APICAL 3 CHAMBER VIEW BASAL INFEROLATERAL :

BASAL ANTEROSEPTAL :

MID INFEROLATERAL ;

MID ANTEROSEPTAL :

APICAL 2 CHAMBER VIEW BASAL ANTERIOR :

BASAL INFERIOR :

MID ANTERIOR ;

MID INFERIOR :

standard deviation of Ts (Ts-SD) ofall the LV segments : Maximal difference in Ts (Ts-diff)between any two the LV segments

MASTER CHART

S No	Age	Sex	NYHA CLASS	duration of symptoms (months)	CAD	DM	HTN	CKD	VALVUALR HEART DISEASE	DCM	ECG QRS WIDTH	EDLV	ESLV	EF	TAPSE
1	33	M	III	8	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	90	172	134	22	16
2	23	M	III	6	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	84	145	102	30	15
3	43	M	III	18	FALSE	FALSE	FALSE	TRUE	FALSE	FALSE	88	156	119	24	12
4	50	M	II	12	FALSE	TRUE	TRUE	TRUE	FALSE	FALSE	92	136	90	34	18
5	58	M	III	15	TRUE	TRUE	FALSE	FALSE	FALSE	FALSE	98	153	103	33	17
6	45	M	II	14	FALSE	TRUE	TRUE	TRUE	FALSE	FALSE	102	162	128	21	15
7	62	M	III	11	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	86	144	93	35	19
8	60	F	II	9	FALSE	FALSE	FALSE	FALSE	TRUE	FALSE	94	132	91	31	17
9	53	F	II	7	FALSE	FALSE	FALSE	FALSE	TRUE	FALSE	100	126	84	33	16
10	46	M	III	6	TRUE	FALSE	TRUE	FALSE	FALSE	FALSE	82	153	96	37	20
11	36	M	III	18	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	104	180	144	19	13
12	42	M	III	16	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	88	170	127	26	16
13	64	M	II	20	TRUE	TRUE	TRUE	FALSE	FALSE	FALSE	90	142	82	35	19
14	36	M	III	6	FALSE	FALSE	TRUE	TRUE	FALSE	FALSE	80	131	83	37	21
15	42	M	II	10	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	98	126	91	28	19
16	57	M	II	6	FALSE	FALSE	FALSE	FALSE	TRUE	FALSE	108	166	112	31	22
17	34	M	III	14	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	102	182	138	24	14
18	64	M	III	9	FALSE	FALSE	TRUE	TRUE	FALSE	FALSE	94	131	86	34	21
19	41	F	III	6	FALSE	FALSE	FALSE	TRUE	FALSE	FALSE	110	139	91	35	18
20	54	M	II	20	TRUE	FALSE	TRUE	FALSE	FALSE	FALSE	108	177	122	31	16
21	53	M	II	13	FALSE	FALSE	FALSE	FALSE	TRUE	FALSE	94	164	103	36	22
22	76	M	III	14	TRUE	TRUE	TRUE	FALSE	FALSE	FALSE	114	146	97	34	16
23	26	F	III	7	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	84	124	84	34	20
24	38	M	II	7	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	90	158	103	35	19
25	44	M	II	16	TRUE	TRUE	FALSE	FALSE	FALSE	FALSE	108	182	128	29	16
26	28	M	III	10	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	104	158	122	23	17
27	35	M	III	9	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	110	181	143	21	13
28	48	M	II	11	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	84	122	79	35	21
29	43	M	II	8	TRUE	FALSE	FALSE	FALSE	FALSE	FALSE	106	162	112	31	18
30	24	M	III	7	FALSE	FALSE	FALSE	FALSE	FALSE	TRUE	78	134	89	33	17

IVMD		intraventricular electromechanical delay												
aortic PET	Pulmonary PET		apical four chamber				APICAL 3 CHAMBER				APICAL 2 CHAMBER			
		SPWMD	basal anterolateral	basal septal	mid anterolateral	mid septal	BASAL INFEROL-	BASAL ANTERO-	MID INFERO	MID ANTE-	BASAL ANTERIOR	BASAL INFERIOR	MID ANTERIOR	MID INFERIOR
112	81	94	135	209	128	202	132	182	131	128	110	108	169	122
88	109	118	175	135	212	134	189	142	137	263	121	175	151	156
121	82	132	186	124	195	138	162	131	129	196	151	118	172	135
95	110	58	142	131	152	124	145	161	122	138	118	143	134	151
108	92	88	128	146	171	143	133	129	150	123	128	110	157	144
124	81	134	194	129	154	133	183	174	123	177	135	134	188	142
98	88	74	140	135	148	114	159	133	115	118	144	151	126	157
104	90	82	130	141	162	145	130	136	154	114	137	119	142	158
84	94	60	134	122	128	118	171	153	148	124	152	163	136	153
92	102	72	152	135	166	145	169	141	127	130	115	134	144	138
126	92	102	175	135	212	134	189	142	137	263	121	175	151	156
128	84	96	173	122	178	127	193	152	124	200	155	121	170	137
78	84	70	132	145	138	124	169	123	125	138	124	152	134	160
102	86	64	128	139	160	125	144	127	162	110	157	129	152	148
96	118	136	144	117	136	121	163	133	133	130	162	144	135	132
124	80	78	129	134	159	136	158	147	125	142	123	117	136	157
106	92	106	141	211	124	184	142	194	128	243	132	144	142	120
100	88	70	121	154	127	133	168	118	136	144	115	163	124	155
94	80	68	133	159	157	113	156	134	160	117	161	124	155	147
114	86	140	154	121	147	135	166	149	132	126	140	152	125	148
106	78	58	136	128	160	135	161	145	122	143	149	125	156	137
126	94	136	130	143	136	127	167	128	121	141	122	156	140	162
76	70	68	137	124	150	118	145	120	163	111	158	131	155	134
84	68	72	142	119	135	131	169	124	151	140	152	158	125	128
116	74	64	134	130	162	130	156	143	131	135	128	114	139	160
128	80	120	127	211	134	224	136	198	154	132	115	117	172	126
124	90	84	168	130	204	124	198	152	128	254	127	184	141	166
86	80	74	122	137	135	129	161	135	159	128	165	140	139	124
126	80	122	143	221	130	212	135	194	119	138	123	112	176	132
94	84	82	125	154	128	134	157	119	143	136	131	160	122	157

:PATIENT CONSENT FORM

Study Details: **ECHOCARDIOGRAPHIC ASSESSMENT OF INTER AND INTRAVENTRICULAR DYSSYNCHRONY IN HEART FAILURE PATIENTS WITH NORMAL QRS DURATION**

Study Centre : **Department of cardiology,**
Madras Medical College and
Rajiv Gandhi Government General Hospital,
Chennai - 600 003.

Patient may check (□) these boxes:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that the investigator of the clinical study, others working on his behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ☐

I hereby give permission to undergo complete clinical examination and diagnostic tests including Electrocardiogram and Echocardiogram. ☐

I hereby consent to participate in this study. ☐

Signature / Thumb impression:

Patient Name and Address: Signature of Investigator:

Place : Date : Study Investigator's Name :

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு: இருதய செயல் திறன் குறைபாட்டில் இருதய அறைகளுக்கிடையே

ஒத்திசைந்த இயக்கமின்மை குறித்த ஓர் ஆய்வு .

ஆராய்ச்சி நிலையம்:இருதயவியல் துறை,

இராஜீவ் காந்தி அரசு பொது மருத்துவமன

மற்றும் சென்னை மருத்துவக்கல்லூரி,

சென்னை – 600 003.

பங்கு பெறுபவரின் பெயர்: **உறவு முறை:**

பங்கு பெறுபவரின் எண்:

பங்கு பெறுபவர் இதனை (√) **குறிக்கவும்**

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களைக் கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவும், மேலும் இது சார்ந்தஆய்வு மேற்கொள்ளும்போதும், இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்துகொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும், அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்துகொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறாக நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு மருத்துவப் பரிசோதனை, இ.சி.ஜி பரிசோதனை மற்றும் இருதய நுண் ஒலி பரிசோதனை செய்ய சம்மதிக்கிறேன் .. ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி .....

கட்டைவிரல் ரேகை:

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம் .....தேதி .....

ஆய்வாளரின் பெயர் .....

ETHICAL COMMITTEE APPROVAL ORDER

INSTITUTIONAL ETHICS COMMITTEE

MADRAS MEDICAL COLLEGE, CHENNAI – 600 003

EC Reg. No. ECR /270/Inst/TN/2013

Telephone No. 044 25305301

Fax 044 25363970

CERTIFICATE OF APPROVAL

To

Dr .T.Viswanathan ,

Post graduate in DM Cardiology,

Department of Cardiology,

Madras Medical College, Chennai 600 003.

Dear Dr. Dr .T.Viswanathan,

The Institutional Ethics Committee of Madras Medical College , reviewed and discussed your application for approval of the proposalEchocardiographic assessment of inter and intraventriculardyssynchrony in heart failure patients with normal QRS durationNo. 29122013.

The following members of the Ethical Committee were present in the meeting held on 11.12.2013 conducted at Madras Medical College, Chennai – 3.

1. Dr .G.Sivakumar , MS FICS FAIS	Chairperson
2. Prof.B.Kalaiselvi , MD Vice Principal, MMC, Ch3	Member Secretary
3. Prof.Ramadevi , Director i/c, Institute of Biochemistry, Chennai	Member
4. Prof .P.Karkuzhali , MD; Prof.Inst .of Pathology, MMC, Ch 3	Member
5. Thiru .S.Govidasamy , BA., BL.,	Lawyer
6. Tmt .ArmoldSaulina , MA MSW	Social Scientist

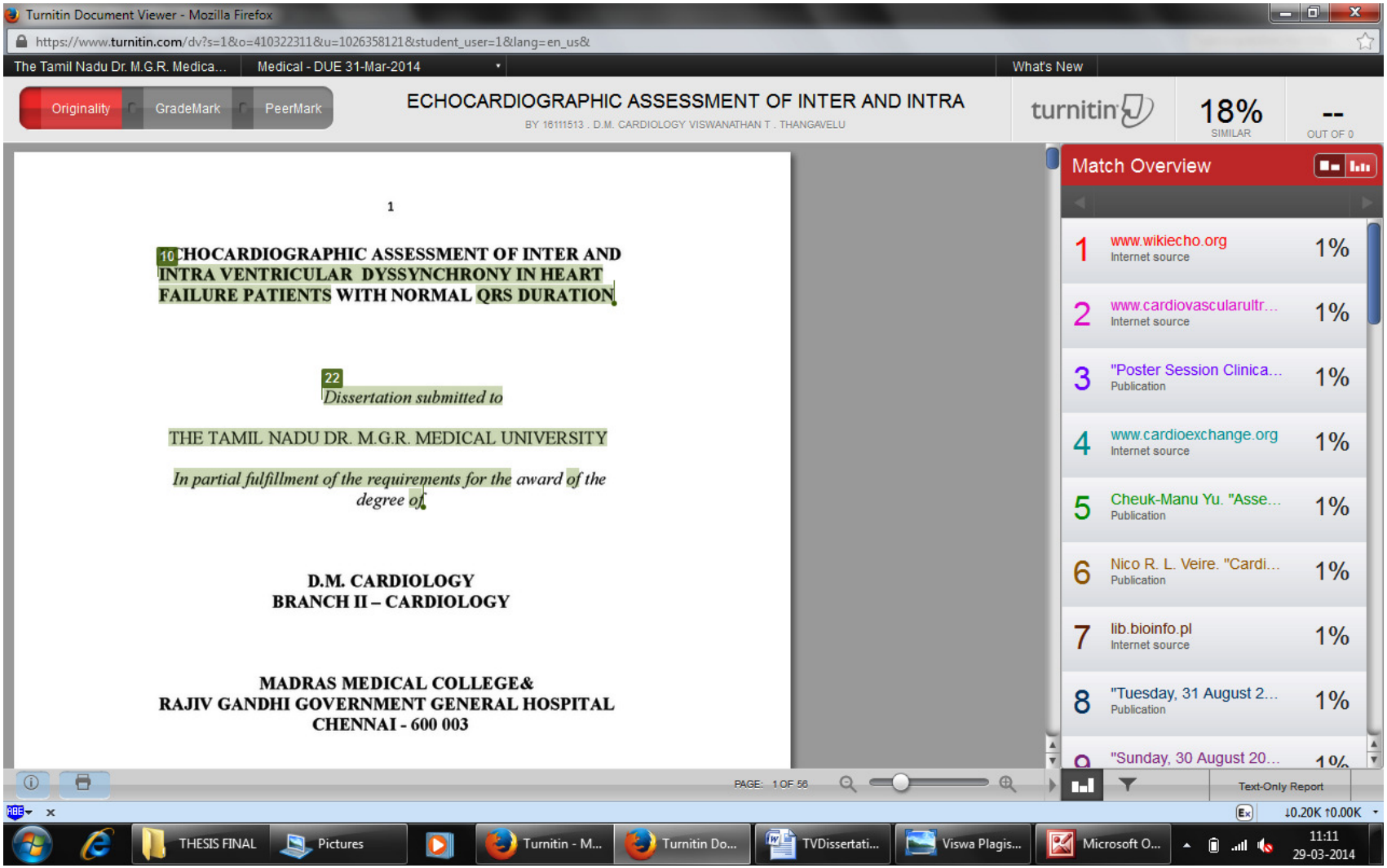
We approve the proposal to be conducted in its present form.
Sd / Chairman & other Members.

The Institutional Ethics Committee expects to be informed about the progress of the study , and SAE occurring in the course of the study , any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

23/12/13

Member Secretary , Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003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Dissertation submitted to
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
In partial fulfillment of the requirements for the award of the degree of
D.M. CARDIOLOGY
BRANCH II – CARDIOLOGY
MADRAS MEDICAL COLLEGE&
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