Original Research Article

Echocardiographic assessment of inter and intra ventricular dyssynchrony in heart failure patients with normal QRS duration

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Abstract

Background: Cardiac resynchronization therapy can improve cardiac function and clinical status in patients with severe heart failure and left bundle branch block. Since in initial studies patients with a wide QRS seemed to benefit the most from biventricular pacing, most of the patients enrolled in these trials had a QRS duration greater than 150 ms. **Aim**: To assess the prevalence of inter and intraventricular dyssynchrony in heart patients with normal QRS duration irrespective of the etiology. **Methods:** 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 were included in the study. All patients underwent detailed Echocardiographic evaluation. The echocardiogram was performed using PHILIPS HD7XE machine. **Results:** Dyssynchrony can be present in severe heart failure. 30 heart failure patients with ejection fraction less than 35% and narrow QRS (less than 120 milliseconds) with duration of symptoms 6 months or more were assessed by detailed Echocardiographic evaluation. Interventricular dyssynchrony was present in 20% of the patients The frequency of intraventricular dyssynchrony in this study was 23.3% based on Ts SD and Ts diff. Among the indices, the correlation between Ts –SD and Ts diff was greater. Intra and interventricular dyssynchrony occur in a significant proportion of heart failure patients with a QRS duration of 120 ms or less. **Conclusion:** Cardiac resynchronization therapy can improve cardiac function and clinical status in patients with severe heart failure and left bundle branch block. Since in initial studies patients with a wide QRS seemed to benefit the most from biventricular pacing, most of the patients enrolled in these trials had a QRS duration greater than 150ms.

Key Word: Pacing, Heart failure, intraventricular dyssynchrony, Echocardiography

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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 occur 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. 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

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with alterations in the local and systemic neurohormonal milieu playing an important role in pathological remodeling and changes at the cellular level. Superimposition of electrical conduction delay and mechanical dyssynchrony over these setting results in additive effects and creates complex pathological changes and increased propensity to arrhythmias[1]. Cardiac dyssynchrony can be atrioventricular, interventricular, and intraventricular. Among these, intraventricular dyssynchrony has the greatest effect on contractile impairment. Cardiac resynchronization therapy affects intraventricular dyssynchrony predominantly.[2] Presently Cardiac resynchronization therapy is recommended in heart failure patients with symptoms refractory to medical treatment, decreased LV ejection fraction and QRS duration of 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 ≤ 35% and QRS ≥ 120 ms, despite Optimal medical therapy (CLASS 1 A recommendation)[3] 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 an 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.[4] However, the relationship of QRS duration to mechanical dyssynchrony may not be parallel as documented by several studies.[5,6] Many heart failure patients with narrow QRS (120ms) may have significant dyssynchrony. On the other hand, not all patients with LBBB may show the correlation between the QRS duration and the magnitude of mechanical dyssynchrony. Cardiac resynchronization therapy and its benefits in heart failure are based on resynchronizing the different regions so that the effects of dyssynchrony are modified. 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 of 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. 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. 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. Several indices have been used for the dyssynchrony assessment using TDI.[7]These include the 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 the difference between the times to peak systolic velocity (Ts) of 12 LV segments. Intraventricular dyssynchrony occurs in heart failure with diverse etiologies. Apart from ischemic causes, other conditions include heart failure associated with chronic kidney disease, Valvular heart diseases (Mitral Regurgitation) and Toxins.

AIM

To assess the prevalence of inter and intraventricular dyssynchrony in heart patients with normal QRS duration irrespective of the etiology.

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 symptoms6 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

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, Rajiv Gandhi 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.

RESULTS

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		Values
Age		45.27±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 ±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 ±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 was151.80 (SD 19.22) ml and the end systolic volumewas105.87 (SD 20) ml.

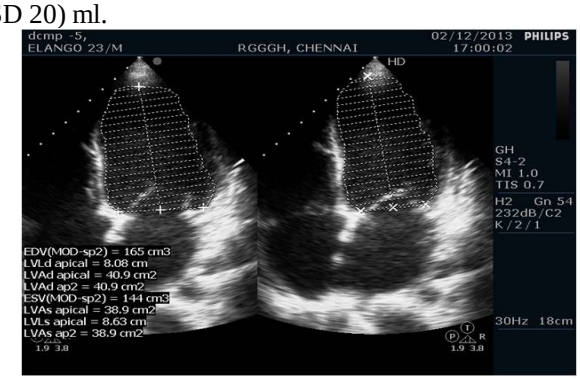

Figure1: Assessment of ejection fraction by modified Simpson's method.

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.

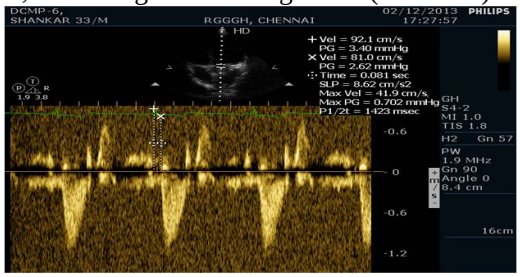

Figure 2: Measurement of aortic pre ejection time.

A difference of more than 40ms 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.

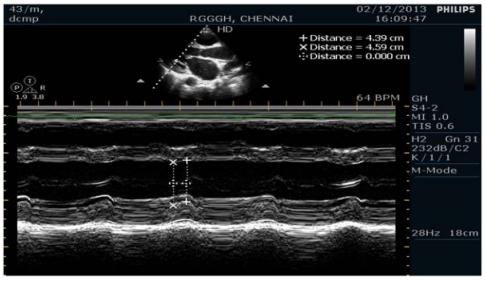

Figure3: Measurement of septal to posterior wall delay

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.

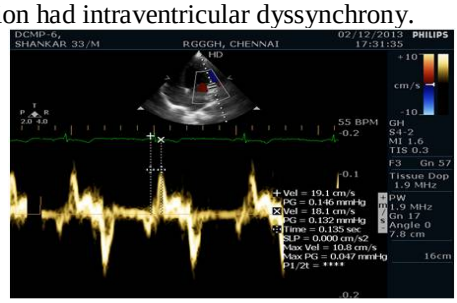

Figure 4: Measurement of Ts of basal anterolateral wall in apical 4 chamber view using tissue Doppler imaging.

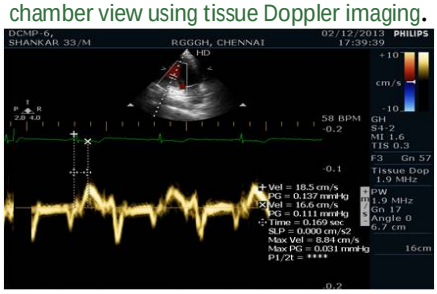

Figure 5: Measurement of Ts of mid inferior wall in apical 2 chamber view using tissue Doppler imaging.

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%)

Relation between Intra Ventricular Dyssynchrony and QRS duration

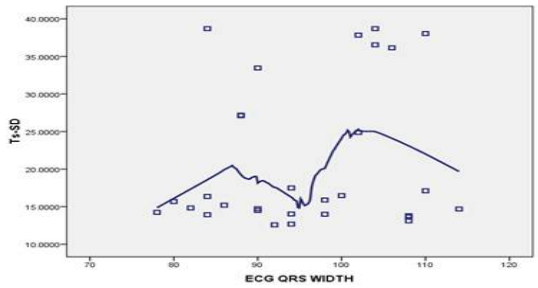

Figure 6: Ts-SD and QRD width in ECG

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 (β = 0.203, 95% CI -0.197 – 0.604, p = 0.308)

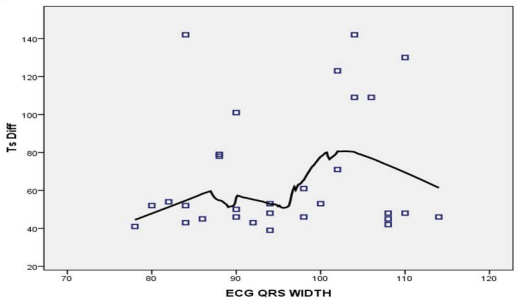

Figure 7: Ts-Diff and QRS width in ECG

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 (β = 0.058, 95% CI-0.061–0.176, p=0.329)

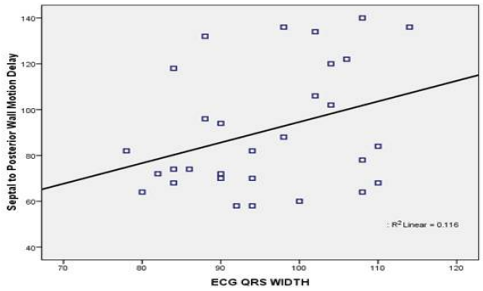

Figure 8: SPWMD and QRS width in ECG

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.

1. **Association Between Inter Ventricular Mechanical Delay And Total Asynchrony Index**

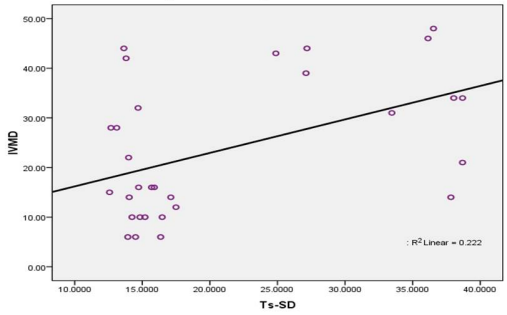

Figure 9: relationship between IVMD and Ts-SD

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 (β=0.329, 95%CI0.091-0.568, p=0.009).

Table 3: Association between Inter Ventricular Mechanical Delay (IVMD) and Total Asynchrony Index

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

There seems to be low association between the IVMD and Ts-SD in the study patients. Pearson's Chi Square: 0.419, p value: 0.603

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*[8] 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 al*[9] 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*[10] 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 by Zahra Emkanjoo *et al*[10] inter ventricular dyssynchrony was present in 26.8% of normal QRS group compared to 42.5% in patients with wide QRS. In a study by Stefano Ghio *et al*[8] interventricular dyssynchrony (defined by the presence of an inter ventricular 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*[11] 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*[9] regarding utility of tissue Dopplervelocity 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 SmitaMehta and Samuel J Asirvatham[12]. 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.

CONCLUSION

Intra and interventricular dyssynchrony occur in a significant proportion of heart failure patients with aQRS duration of 120 ms or less. The prevalence of intraventricular electromechanical dyssynchrony was 23% and interventricular dyssynchrony 16%. 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. There is no association between the QRS duration and the dyssynchrony parameters in the study. There is no association between interventricular dyssynchrony and intraventricular dyssynchrony.

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