Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

A Study of Prevalence of Mechanical Dyssynchrony in Patients With Varying QRS Interval And Its Correlation With Left Ventricular Function Using Tissue Doppler Technique.

Upendra Narayan Singh[2], Kalpana Kumari Singh[1], Virendra Prasad Sinha[3]

[1]Assistant Professor, Department of Cardiology, Patna Medical College, Patna.
[2]Resident, Department of physiology; Narayan Medical College, Sasaram
[3]Associate Professor, Department of Cardiology, Patna Medical College, Patna.

Received: June 2017
Accepted: June 2017

ABSTRACT

Background: Cardiac resynchronisation therapy is now established modility of treatment of dilated cardiomyopathy with wide QRS (LBBB) duration who are refractory to medical therapy. However a significant a significant number of patients are responder to this therapy also. On the contrary about 40% patient's dilated cardiomyopathy having narrow QRS do better with cardiac resynchronisation therapy. However the true prevalence of interventricular and intraventricular dyssynchrony in broad set of dilated cardiomyopathy and its relation with LV function has not been assessed using newer techniques. The present study is designed to assess the prevalence of interventricular and intraventricular dyssynchrony in dilated cardiomyopathy patients with varying QRS duration also, its relation with left ventricular function with tissue Doppler techniques. **Methods & Results:** Fifty nine consecutive patients of dilated cardiomyopathy having ejection fraction ≤45% with varying qrs duration and 20 patients having normal left ventricular function with wide QRS duration were studied. The patients were then grouped as group A dilated cardiomyopathy having wide qrs interval , group B dilated cardiomyopathy with narrow QRS and group C having normal left ventricular function with left bundle branch block. The interventricular and intraventricular` were assessed in apical four chamber , 2 chamber and long axis view Using colour coded B mode tissue Doppler technique. Data were analysed offline and the standard reported parameters were used for defining interventricular and intraventricular dyssynchrony. The interventricular dyssynchrony was present in significant proportion of patient of group a, group B and group C. It was present was present in 78 % of group A, 68.7% in group B and 60 % of group C. The prevalence of intraventricular dyssynchrony was present was present in 68.7 % of group A, 48% in group B and 5 % of group C. There was significant positive correlation between QRS width and intraventricular dyssynchrony was observed (r =.342, p=0.008) in dilated cardiomyopathy patients irrespective of QRS duration. There was statistically significant interaction when intraventricular dyssynchrony and QRS width (r = 0.652, p<.001) analysed in among group A, however it was no significant in group B (P=0.68) individually. There was significant correlation between LV dyssynchrony and left ventricular ejection fraction. r = -.303 p=0.014 as this association is no as robust as the QRS width. **Conclusion:** We concluded that there is quite good correlation between left ventricular dyssynchrony and QRS duration in patients of dilated cardiomyopathy. There is also weak correlation between intraventricular dyssynchrony and left ventricular ejection fraction irrespective of QRS duration.

Keywords: Cardiac Resynchronisation, Doppler, Left Ventricular Function.

INTRODUCTION

Heart failure is a major health problem in India as well as western world.[1] Treatment of heart failure remains one of the major challenges in health care practice despite major advances in medical therapy.[2] In recent decades there has been remarkable improvement in survival due to medical therapy and newer treatment modalities like cardiac resynchronisation therapy and implantable cardiac defibrillator.[3] Cardiac resynchronization therapy (CRT) is an important advance for heart failure patients with depressed left ventricular (LV) ejection fraction and prolonged electrical activation. Patients have benefited from CRT by experiencing improvements in exercise capacity, quality of life, ventricular function, and survival.[4] Most of contemporary trials considered only patients with severe heart failure, left ventricular ejection fraction (LVEF) 35%, and a wide QRS complex (as marker of cardiac dyssynchrony).[5] The definition and/or the evaluation of cardiac dyssynchrony are still a matter

Name & Address of Corresponding Author
Dr. Upendra Narayan Singh
Asst professor,
Department of Cardiology,
Patna medical College,
Patna.

of debate.[5] But the major issue regarding CRT is that, when patients are selected according to the QRS duration on surface ECG, approximately 30% do not have a beneficial response. It is widely believed that abnormalities of regional mechanical activation, known as LV dyssynchrony, are the underlying pathophysiology that is improved by CRT.[6] This might be because mechanical dyssynchrony may not necessarily relate to electrical dyssynchrony (width of QRS).[7, 8] i.e. some patients with wide QRS may not exhibit LV dyssynchrony whereas others with narrow QRS duration may demonstrate significant LV dyssynchrony.[9-10]

From both experimental and clinical imaging studies, it has become evident that cardiac dyssynchrony is important for response to CRT. Dyssynchrony can occur at 3 levels:

- Atrioventricular dyssynchrony
- Interventricular dyssynchrony
- Intraventricular (LV) dyssynchrony

The weight of current evidence favours mainly Intraventricular or LV dyssynchrony as most associated with response to CRT and only few studies demonstrated predictive response to CRT in Intraventricular dyssynchrony.[8]

The present study was planned to assess the prevalence of Interventricular and Intraventricular dyssynchrony in broad sets of patients of dilated cardiomyopathy with varying QRS duration, including patients with narrow and broad QRS and varying left ventricular function using tissue Doppler and strain imaging techniques.

MATERIALS AND METHODS

Patients

Consecutive patients referred to our department with clinical diagnosis of dilated cardiomyopathy with heart failure from July 2011 to January 2012 has been selected in our study on the basis of following inclusion criteria;-all patients having LV systolic systolic function i.e. left ventricular ejection fraction< 45% . We excluded patients with

1. Non sinus rhythm
2. previous pace maker implantation
3. Inability to perform technically acceptable echocardiogram
4. Isolated right heart failure
5. Right bundle branch block
6. Presence of valvular stenotic or regurgitant lesion

Additionally there was another subsets of patients having wide QRS, left bundle branch morphology having preserved left ventricular functions that serves as controls so as to study the relation of ventricular dyssynchrony to LV function if any independent of QRS duration. A written informed consent was taken from all patients. These patents were studied in 3 broad categories

A. Dilated cardiomyopathy with left bundle branch block
B. Dilated cardiomyopathy with narrow QRS (without LBBB)
C. Normal left ventricular functions with left bundle branch block

Electrocardiography

Standard 12 lead electrocardiograms was acquired at the speed of 25mm/sec and a scale of 1omm/mv. The measurements of PR interval and QRS duration were recorded from the surface leads demonstrating the greatest values and the assessment of QRS axis and morphology were performed by an experienced observer who was blinded to echocardiographic characteristics of the patients. The typical ECG feature of left bundle branch block(LBBB) taken was QRS duration of ≥120 ms, having no q wave but slurred/broad R waves in lead in I , aVL, V6 and rS or QS deflections in lead V1. Patients with LBBB type Intraventricular lead conduction delay were also included.

Echocardiography

The echocardiography examination was performed on ALOKA PROSOUND α10 System equipped with S4 mutifrequency transducer with software for tissue Doppler, strain and strain rate technique. Recording was done by performed by single operator in left lateral position so as to avoid inter observer variability. A complete echocardiography was performed in apical four chamber,2 -chamber and long axis view was done and recorded .The myocardial walls is aligned parallel to the Doppler beam to minimize the angle of insonation, and the frame rate was optimized from 100 to 140Hz. Pulsed Doppler images of the aortic outflow tract were acquired for definition of systole. The measurement was being carried out for minimum of 3 cardiac cycles. Manual adjustments were made so that the regions of interest had the most reproducible peak velocities

Measurement of inter-ventricular and intra-ventricular delay

The following conduction delay measurement was done.

1. Interventricular delay

Interventricular dyssynchrony refers to a prolonged delay between the onset of RV and LV activation. Intraventricular dyssynchrony is determined by placing sample volumes in RV basal free wall and LV basal lateral walls and determining the time difference in the onset of RV and LV walls mechanical activation. A minimum of 3 reading was taken, and was averaged. The significant interventricular dyssynchrony was defined when the delay between these walls >40 milli seconds.

2. Intraventricular dyssynchrony

Six basal segments were studied and analysed. To determine Intraventricular dyssynchrony, sample volume (6mm x 6mm) was placed at basal septum and lateral wall, anterior wall and inferior wall and anterior wall and posterior wall. In apical 4 chamber, apical 2 chamber view and long axis view. The mid segment was not studied, as the velocity curves were of poor quality because these segments were closure to apex and peaks of these curves were not so conspicuous. So in order to avoid error, the mid segment was not studied.

These 2 published dyssynchrony parameters were used to assess Intraventricular dyssynchrony. (1) The basal septum -lateral delay (SLD) in time to peak systolic velocity measured with colour coded tissue Doppler modality.

(2) The maximum difference in times to peak systolic velocity between any 2 of the basal septal, lateral, anterior, and inferior LV segments (Max Diff)

A significant delay was defined when the septolateral delay or the maximum delay between the 2 opposing wall was greater than 65 milliseconds. Patients meeting either of the 2 criteria were taken as significant dyssynchrony.[11]

A criteria combined Intraventricular and interventricular delay was also calculated. The combined delay more than 110 milliseconds are considered significant for predicting response to cardiac resynchronisation therapy.

Methods for assessing Intraventricular and interventricular delay

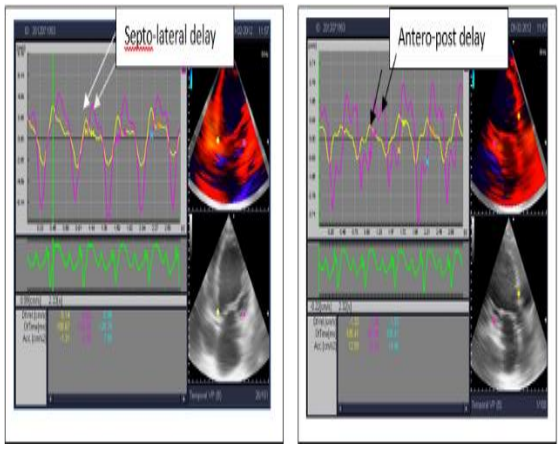


Figure 1: Assessment of intraventricular dyssynchrony with tissue Doppler technique (a) septolateral delay of 120 ms (b) there is antero posterior delay of.

Left ventricular function assessment

The following parameters were evaluated: left ventricular end diastolic volume (LVEDV); Left ventricular end systolic volume (LVESV) and ejection fraction was calculated by modified biplane Simpson's rule. Mitral regurgitation and tricuspid regurgitation were graded as mild, moderate or severe.

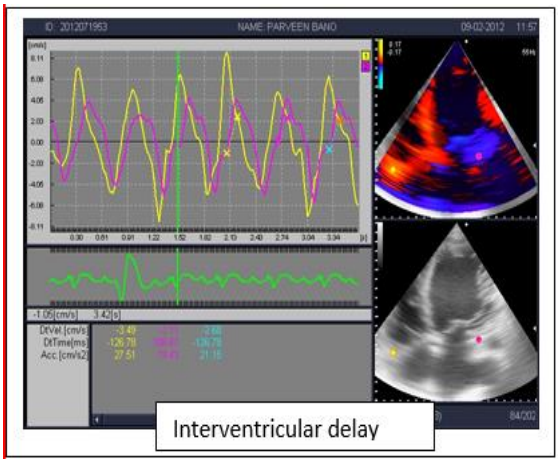


Figure 2: Assessment of interventricular delay .There is delay of.

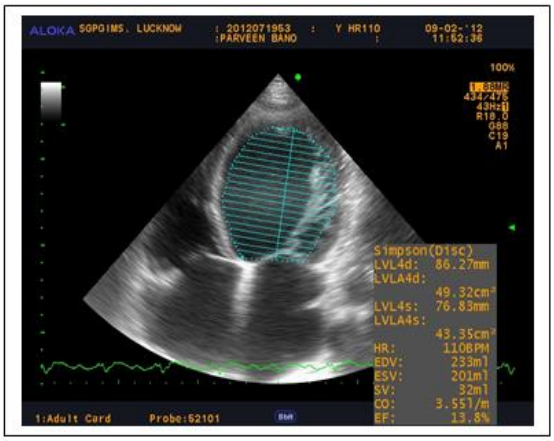


Figure 3: Assessment of left ventricular ejection fraction by simpson´s rule.

Statistical analysis

All statistical analysis was done one spss program for window version 17.0. The data are shown as mean values, SD for the continuous variables (or median and inter-quartile ranges (IQR) for skewed distributions) and as absolute or relative frequencies for categorical variables. Due to the small number of patients with hypertension, such patients were considered together with DCM patients for statistical analysis. Patient's characteristics were compared by means of one way analysis of variance (overall comparison) and Bonferroni test (post hoc pairwise comparisons) in case of continuous variables; the Fisher exact test was used to compare categorical variables. A general linear model was used to evaluate the association between Intraventricular dyssynchrony and QRS groups, while controlling for patient's baseline characteristics (age, ejection fraction, mitral regurgitation, left ventricular filling); such characteristics were selected on clinical grounds.

RESULTS

A total of 79 patients were finally analysed. The mean age was 53.9±8.6 years. All of patients had non ischemic aetiology of HF and about 92% were idiopathic and rest of the patient were hypertensive cardiomyopathy and idiopathic in aetiology. Table 1 shows the baseline clinical demographics in these 3 study group and the age, sex, aetiology of cardiomyopathy and medication taking were not significantly different in group A and B. The NYHA functional class, end diastolic volume, end systolic volume, ejection fraction were similar in these groups. The group C served as control with normal ejection fraction and left bundle branch morphology. Table 2 and Table 3 demonstrate the magnitude of Intraventricular delay between two opposing walls, magnitude of Intraventricular and interventricular delay.

Table 1. Demographic characteristics of patients in different groups.

		Reduced Ef, Qrs.>120 (A)	Reduced Ef, Qrs<120 (B)	Normal Ef, Qrs.>120 (C)	P value
Age of the patient in year		55.3±8.6	53.7±8.8	52.1± 8	P=0.4
NYHA functional class	I	-	-		
	II	53.1	55.6		P=0.68
	III	37.5	40.7		P=0.67
	IV	9.4	3.7		P =ns
QRS width in millimeter		136.7± 8.8	109.56±8.0	133.00±6.6	P<0.005(A&B) P=0.34(A&C)
LVend diastolic diameter		64.8±8.6	63.4626±7.322	49.05±4.7	P=ns(A&B) P =0.00(A&C)
LVend systolic diameter		49.13± 9.5	48.35± 7.6	30.40±6.2	P=ns(A&B) P =0.00(A&C)
left ventricular ejection fraction		27.25± 8.7	31.37± 7.2	57.40± 6.3	P =0.13(A&B) P =0.00 (A&C/B&C)
Etiology	Idiopathic	90.6	92.5		
	Hypertensive	6.3	3.7		
	Alcoholic	3.1	3.7		
Diuretics		81.3	85	0	
ACE inhibitor		73.3	74	-	
Digoxin		53.3	43	.	
Beta blocker		75	62	10	
Nitrates		4.2	4.3	-	
Aspirin		10.3	7.7	-	

Table 2: Magnitude of intraventricular and interventricular delay.

Grouping Of Patients According To Ef And Qrs Duration	Reduced Ef, Qrs>120	Reduced Ef, Qrs<120	Normal Ef, Qrs.>120	P Value
Intra ventricular delay	80.53±51	58.11 ±31	49.2±17.6	P=0.019(A&C) P=0.05(A&B) P=1.0 (B&C)
Interventricular delay	81.1± 54	58 ±33	53.2±24	P=0.123(A&B) P=0.07(A&C) P= NS(B&C)

Prevalence of interventricular and inraventricular delay

Interventricular delay

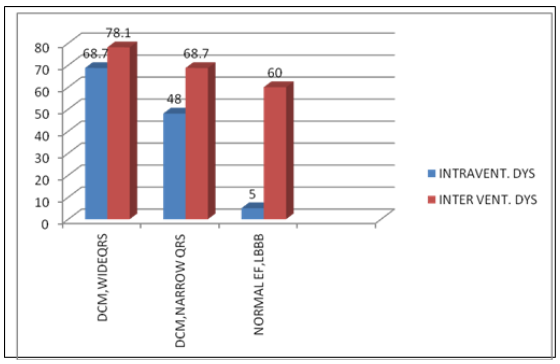
The interventricular dyssynchrony was present in significant proportion of patient of group A, group B and group C. It was present was present in 78 % of group A, 68.7% in group B and 60 % of group C.The mean QRS duration in these groups were 136.69± 8.8 ms 109.56±8.0 ms and 133.00±6.601. The magnitude of inter ventricular delay was 80 ±, 54 ms, 57.9 ±33.6 and 53±24 ms respectively in these groups. There was significant relation between interventricular dyssynchrony and QRS duration (p=0.03).Table 4 shows the prevalence (%) of intraventricular and interventricular delay among different patents group.

Table 3: Delay between opposing walls of left ventricle

	Group A	Group B	P value
Septolateral delay	74.3±51.4	50.2±31.5	P=0.04
Antero-inf delay	64.6±44.4	45.5±26	P=0.05
Antero-post delay	63.7±35.4	45.5±26	P=0.013
Max. Difference between two opposing walls	80.538±51	58.10±31	P=0.050

There were significant numbers of patients in group A and group B had intraventricular delay. The prevalence of intraventricular dyssynchrony was present was present in 68.7 % of group A, 48% in group B and 5 % of group C. There was significant positive correlation between QRS width and intraventricular dyssynchrony was observed (r =.342 , p=0.008) in dilated cardiomyopathy patients

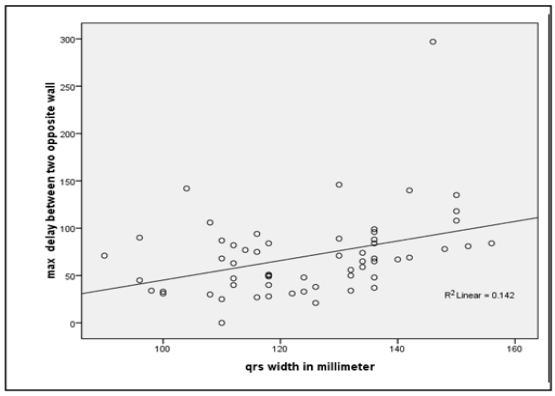
irrespective of QRS duration. There was statistically significant interaction when intraventricular dyssynchrony and QRS width (r = 0.652, p<.001) analysed in among group A, however it was non significant in group B (P=0.68) individually. The magnitude of intraventricular delay was79.8±51 and 56.0±30.0 (P=0.050) ms in these groups.



Intraventricular delay

Subgroup analysis of groupA revealed that intraventricular dyssynchrony was much more prevalent in those patients having QRS duration was >140 milliseconds and intraventricular dyssynchrony has significant positive robust correlation with QRS width. Intraventricular dyssnchnony was present in all nine (100%) patients in this group. On the otherhand dyssynchrony was much less prevalent (14.3 %) in DCM patients with wide QRS but LBBB type of intraventricular conduction delay. Although the mean QRS duration was 128±4.56 in this group which was not significantly different from parent group i.e. group A. The delay between sepal and lateral delay was most frequent in the patients having intraventricular dyssynchrony. The histogram demonstrates intraventricular dyssynchrony in different subgroups and correlations amongst these subgroups.

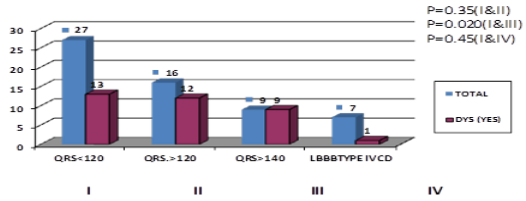
Scatter diagram depicting relation between maximum delay and QRS width



Scatter diagram-depicting relation between maximum delay and QRS width

LV mechanical dyssynchrony and Left ventricular ejection fraction

There was significant correlation between LV dyssynchrony and left ventricular ejection fraction. r = -.303 p=0.014 as this association is no as robust as the QRS width



DISCUSSION

The present study illustrates that interventricular and intraventricular dyssynchrony is prevalent in broad categories of patients. The interventricular dyssynchrony is frequent in heart failure patients and normal left ventricular functions with wide QRS. The interventricular dyssynchrony is present in 78% of patients in dilated cardiomyopathy with wide QRS and 66% of patients with narrow QRS interval and 60 % of patients with normal left ventricular function and wide QRS having LBBB morphology. Left ventricular intraventricular dyssynchrony is present not only in impaired left ventricular function with left bundle branch morphology (66%) but an also in significant proportion of patients with narrow QRS interval (48%). Only 1 patient in LBBB with normal LV function had significant intraventricular delay. However, there were significant number of patients has interventricular delay in this group which is purely due to delayed conduction. Only 1 in seven patients having decreased ejection fraction with left bundle branch type of IVCD had intraventricular delay. This study demonstrated that, not only QRS duration and morphology were predictors of dyssynchrony but also the poorer left ventricular ejection fraction was independently associated with mechanical dyssynchrony. The prevalence of interventricular and intraventricular study is similar to contemporary studies. This study also provides the insight in to the factors predictors of mechanical dyssynchrony.

As observed in this study that LV dyssynchrony is much more prevalent among the patients with wider QRS complexes (>140ms) having typical left bundle branch block. On the contrary intraventricular conduction delay on surface electrocardiogram is negatively associated with intraventricular dyssynchrony despite having wide QRS complexes. This observation partially explains why beneficial response to CRT is not uniformly present when the patients are selected alone on the basis of surface electrocardiogram. Conversely, as observed in this study, it was also demonstrated in many studies that

20% -50% of heart failure patients with QRS duration (<120ms) may also exhibit LV dyssynchrony and these patients may benefit from CRT.[12-14] Recently, the RethinQ (Cardiac Resynchronization Therapy in Patients with Heart Failure and Narrow QRS) study was published looking at CRT in 172 patients with heart failure (EF 35%), and a narrow QRS complex, but With mechanical dyssynchrony, with the majority of patients (96%) enrolled based on the opposite wall delay method by colour tissue Doppler imaging (15). In study, CRT did not result in a significant change in peak oxygen consumption (primary end point), Minnesota Living with Heart Failure score, 6-min walk, and LV volumes/EF at 6 months. The potential reasons for these results include problems with the echocardiographic methods used to identify patients, issues with lead placement as it relates to the site with latest contraction and scar tissue, and the actual possibility that dyssynchrony in this population is not due to a conduction delay that can be corrected by CRT (as stated in the Viewpoint by Kass).[16]

CONCLUSION

This study demonstrated that echocardiographic left ventricular (intra-ventricular) dyssynchrony was highly prevalent in patients with wider QRS duration(>140 ms) as compared with those with QRS duration (120-140 ms) and narrow QRS duration in patients of heart failure using tissue Doppler techniques (opposite wall delay) .QRS duration on surface electrocardiogram was most significantly associated with echocardiography intraventricular dyssynchrony(r= .342 ,p=0.008) . Poor left ventricular ejection fraction was also independently associated with higher(r=- 0.303 ,p=.0140 left ventricular dyssynchrony and intraventricular conduction delay . Although septum-lateral delay was commonest form of left ventricular dyssynchrony observed, others like antero- inferior and antero posterior delay were also common. This study can partially explain non responsiveness to cardiac resynchronisation therapy when patients having wide QRS selected solely on surface electrocardiogram whether as 20-50% of heart failure patients having narrow QRS were well responsive to cardiac resynchronisation therapy. Non responsive to CRT despite of documented dyssynchrony on echocardiography may be due to technicals reasons in performing echocardiogram , non placement of lead to site of latest mechanical activation or scar in the area having latest delay.

Limitations: As this study is only observation and all patients did not undergone cardiac resynchronisation based on dyssynchrony observed due to many reasons.

Acknowledgments

We are grateful to the entire staffs of non invasive laboratory (echocardiography laboratory staff), department of cardiology, sanjay Gandhi post graduate institute of medical sciences, for facilitating this study.

REFERENCES

1. ClelandJGF, The heart failure epidemic: exactly how big is it? Eur heart journal ,2001;22;623-636.
2. Zannad F, Briancon S,Juillie´re Y et al incidence ,clinical and etiologic features and outcomes of advanced chronic heart failure;the EPICAL study ,J Am coll cardiology 1999,33; 734-42
3. Hunt S A, Abraham WT, Chin MH, et al. Guidelines for the diagnosis and management of heart failure in adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2009; 53:e1–90
4. Cleland J, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med 2005;352:1539 – 49.
5. The Task Force for Cardiac Pacing and Cardiac Resynchronization Therapy of the European Society of Cardiology. Guidelines for cardiac pacing and cardiac resynchronization therapy. Eur Heart J2007;28:2256 – 95
6. Bax JJ, Abraham T, Barold SS, et al. Cardiac resynchronization therapy part 1—issues before device implantation. J Am Coll Cardiol2005;46:2153– 67.
7. Leclarcq C, Faris O,Tunin R et al.systolic improvement and mechanical resynchronisation does not require electrical dyssynchrony in dilated failing heart with left bundle branch block. circulation 2002,106: 1760-63.
8. Kass DA , predicting cardial resynchronisation response by QRS duration:the long and short list of it.j am coll cardiol 2003;42:2125-27.
9. Achilli A, Sassara M, Ficilli S,et all.long term effectiveness of cardiac resynchronisation therapyin patients of refractory heart failure and ‘’narrow’’QRS .j. am coll cardiol 2003;42:2117-24.
10. Rouleau F, Merheb M, Geffroy S, et al. Echocardiographic assessment of the interventricular delay of activation and correlation to the QRS width in dilated cardiomyopathy. Pacing Clin Electrophysiol 2001;24: 1500 – 6.
11. Baxx JJ, Bleeker GB Marwick TH et al left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronisation therapy. J Am Coll Cardio l2004;44:1834-1840
12. Bleeker GB, Schalij MJ, Molhoek SG, et al. Relationship between QRS duration and left ventricular dyssynchrony in patients with end-stage heart failure. J Cardiovasc Electrophysiol 2004:15:544
13. Yu CM, Lin H, Zhang Q, Sanderson JE. High prevalence of left ventricular systolic and diastolic asynchrony in patients with con-gestive heart failure and normal QRS duration. Heart 2003;89:54 –60.
14. Bleeker GB, Schalij MJ, Molhoek SG, et al. Frequency of left ventricular dyssynchrony in patients with heart failure narrow and a wide QRS complex. Am J Cardiol 2005;95:140 –2
15. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med 2007;357:2461–71.
16. Kass DA. An epidemic of dyssynchrony: but what does it mean? J Am Coll Cardiol 2008;51:12–7.

How to cite this article: Singh UN, Singh KK, Sinha VP. A Study of Prevalence of Mechanical Dyssynchrony In Patients With Varying QRS Interval And Its Correlation With Left Ventricular Function Using Tissue Doppler Technique. Ann. Int. Med. Den. Res. 2017; 3(5):ME15-ME21.

Source of Support: Nil, **Conflict of Interest:** None declared