RELATIONSHIP BETWEEN VENTRICULAR ASYNCHRONY AND QRS DURATION IN PATIENTS WITH LEFT VENTRICULAR SYSTOLIC DYSFUNCTION

AKHTERUZZAMANM M[1], RAHMAN A[2] , RAHMAN M A[3] , AMIN R[4] , MIAH MNA[5], KHAN A. R[6],CHOWDHURY T.A[7] , HOSSAIN A[8], KASHEM M.A[9]

Abstract:

Background: *There are variable degree of asynchrony in end-stage heart failure patients with varying QRS widths and LV function. The study was based on evaluation of relationship between ventricular asynchrony and QRS duration in patients with left ventricular systolic dysfunction in Bangladesh.*

Methods and materials: *This work was carried out in the department of cardiology, Sir Salimullah Medical College, Mitford Hospital, Dhaka from September 2010 to August 2011. 103 patients were selected on the basis of inclusion and exclusion criteria as the study sample. After evolution by history, clinical examination and echocardiography and Tissue Doppler imaging were done in all selected patients by two cardiologists who were blinded to ECG report. Both interventricular & intraventricular conduction delay were measured in all patients of three groups.*

Result: *Interventricular asynchrony by measuring interventricular mechanical delay (IVMD) was greater in Group-II (45.15±26.36) and Group-III (40.92±30.77) compared to Group-1 (23.65±13.58). So step-wise increase in IVMD was noted over three groups & it was statistically significant (P<0.001). But Linear regression demonstrated weak relation between QRS duration & IVMD (Y=0.314x+7.61, n=103, r=0.372, p=0.000) though widely scattered data around the identity line was observed. Intraventricular asynchrony by measuring Septal to post wall motion delay (SPWMD) in msec was also lowest in narrow QRS group compared to others (P>0.05). Linear regression failed to find any relation between QRS duration and Septal-to-posterior wall delay among the patients (r=0.199, p=0.044). Though the magnitude of Lateral-to-Septal delay (LSD) was gradually increased among the groups but it was not significant (P>0.05). No relation was found between QRS duration and Lateral-to-Septal delay(r=0.152, p=0.126). Using the cut off value 60 ms, this study found 65.4% patients of wide QRS group (>150ms) had significant Intraventricular asynchrony & 31% patients of narrow QRS group showed significant asynchrony.*

Conclusion: *The main result of this is the QRS width appears to be poorly correlated with the presence of inter-V and intra-LV electromechanical asynchrony. This study also suggest that, interventricular asynchrony may be grossly identified by the presence of a wide QRS on surface ECG but that, more sophisticated imaging techniques are needed to find out Intraventricular asynchrony.*

Key words: *Ventricular asynchrony, QRS duration, Left ventricular systolic dysfunction.*

Introduction:

Heart failure due to left ventricular systolic dysfunction (LVSD) is a common, costly, disabling and life-threatening condition. Around 1, 20,000 hospital admissions per year are due to LVSD in the UK[1]. The survival rate of LVSD from the time of diagnosis is 67% at 1 year and 24% at 3 years. As LVSD often carries a worse prognosis than several of the common cancers, it is important that patients who present to their family physician with symptoms suggestive of LVSD are identified and offered appropriate treatment[2].

Heart failure can be classified into two broad categories: HF with LV systolic dysfunction and HF with preserved systolic function termed diastolic

1. Registrar, Department of Cardiology, Bangladesh Medical College Hospital, Dhaka
2. Registrar, Department of Neurology, Sir Salimullah Medical College Mitford Hospital, Dhaka
3. Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka.
4. Associate Professor, Department of Medicine, Dhaka Medical College , Dhaka
5. Assistant Professor, Department of Medicine, Sir Salimullah Medical College, Dhaka
6. Assistant Professor, Department of Cardiology, Sir Salimullah Medical College, Dhaka
7. Assistant Professor, Department of Cardiology, Sir Salimullah Medical College, Dhaka
8. Department of Neurology, Dhaka Medical College Hospital, Dhaka
9. Department of Medicine, Sir Salimullah Medical College Mitford Hospital, Dhaka

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dysfunction. The systolic dysfunction means inability of LV to eject blood into high-pressure aorta that means reduced ejection fraction. The term diastolic dysfunction means that the ventricle cannot accept blood at its usual low pressure ventricular filling is slow, delayed, or incomplete unless atrial pressure increases consequently [3].

LV dysfunction is characterized by a change in preload and after load, decrease in myocardial contractility, and increase in diastolic filling pressures [4]. Changes in preload and after load have been characterized by LV remodeling with an increase in the size of left ventricle and a change in LV geometry. Generally, LV diastolic wall stress is used as parameter for preload and LV end-systolic or mean-systolic wall stress as measure for after load. More commonly, the volume-derived contractility parameters are used, such as cardiac index, stroke work index, or preload recruit able stroke work. The most useful parameter in daily practice is the LV ejection fraction, which is the parameter used most frequently for differentiating between systolic and diastolic dysfunction. An ejection fraction of more than 50 percent is considered to be normal, an ejection fraction between 35 to 50 percent is moderately depressed, and an ejection fraction below 35 percent represents a severely depressed systolic pump function. Many of the large clinical heart failure trials are based on these definitions and different therapeutic interventions are dependent on the LVEF, such as the implantation of an ICD & Biventricular pacing [5].

In the developing countries like Bangladesh with increase of life expectancy from 41 to 61 years and control of common infectious diseases and improvement of life style, cardiovascular diseases as well as mortality caused by it is showing an increasing trends [6]. A hospital based cross sectional study was done at a tertiary cardiac hospital in Dhaka city. Hospital medical records of 14,009 patients admitted between January 2005 and August 2006 were reviewed and 1970 patients with the diagnosis of Heart Failure were identified. Relevant etiological information and socio demographic data were abstracted from the hospital record files. The mean age of hospitalized HF patients is remarkably lower than other related studies done abroad. The single most common etiology for HF is ischemic heart disease in this population. Hypertension is the most common risk factor [7].

Another study in National institute of Cardiovascular Diseases, Dhaka, Bangladesh showed that heart failure is most commonly prevalent in the 50-59 years age group. The commonest cause of heart failure was ischemic heart disease (44.97%) followed by hypertension (22.96%) and valvular heart disease (21%). Among heart failure patient 67% had left heart failure and 33% had right heart failure [8].

There is however no large study which has analyzed the true prevalence and degree of asynchrony in end-stage heart failure patients with varying QRS widths and LV function. We still do not know whether there is a link between interventricular and Intraventricular asynchrony, to what extent they are related to QRS morphology, to etiology of the disease or to the degree of left ventricular dysfunction. Focusing these issues is not only a matter of pathophysiological relevance but it is also important to solve the clinical problem of the identification of patients most likely to respond to cardiac resynchronization therapy. The present study was therefore planned to assess the relationship between QRS duration on surface ECG and ventricular asynchrony in large group of patients with both narrow and wide QRS complexes and varying degree of LV dysfunction using noninvasive 2D, M-mode echocardiogram, pulse-wave Doppler, and pulse-wave tissue Doppler imaging.

Methods:

It was a Cross sectional study in the Department of Cardiology, Sir-Salimullah Medical College Mitford Hospital, Dhaka from September 2010 to August 2011. Total103 consecutive patients with left ventricular systolic dysfunction & symptomatic (NYHA class III-IV) on the basis of the inclusion and exclusion criteria were studied. Patients of acute myocardial infarction were excluded by ECG and biomarkers. Inclusion criteria: Patients above 18 years of either sex with symptomatic heart failure (NYHA Class III or IV), etiology due to Ischeamic Cardiomyopaty or non Ischeamic Dilated Cardiomyopathy and LVEF <40% by 2D echocardiogram. Exclusion criteria: Patients with non sinus rhythm, Predominant diastolic dysfunction & vulvular heart disease, previous pacemaker implantation, acute coronary syndrome (ACS) in last three months and acute heart failure. Based on QRS duration the selected patients were then grouped as Group-1 narrow QRS group (QRS width <120 ms), Group-II intermediate QRS group (QRS width 120-150ms) & Group-III wide QRS group (QRS width >150ms). After proper evaluation by history and clinical examination ECG and Echocardiography were done by two cardiologists. Cardiologists who done the echocardiography were blinded to the electro-cardiographic characteristics and also without knowledge of the clinical status of the patient.

Assessment of Interventricular Asynchrony: The aortic pre-ejection time was measured from the beginning of QRS complex to the beginning of the aortic flow velocity curve (Q-AV) recorded by pulsed-wave (PW) Doppler in apical 5-chamber view. The pulmonary pre-ejection time was measured from the beginning of QRS complex to the beginning of the pulmonary flow velocity curve (Q-PV) recorded in the left parasternal view. The difference between the two values determined the interventricular mechanical delay (IVMD); an IVMD>40 ms was considered as the cut-off value for interventricular asynchrony[9, 10, 11].

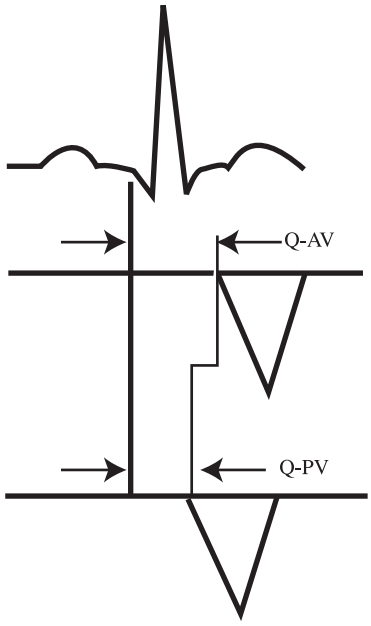

Fig.1. *Assessment of Interventricular mechanical delay by Doppler echocardiography. (Q-AV=Q to Aortic flow, Q-PV=Q to pulmonary flow) IVMD is calculated by subtracting Q-PV from Q-AV*

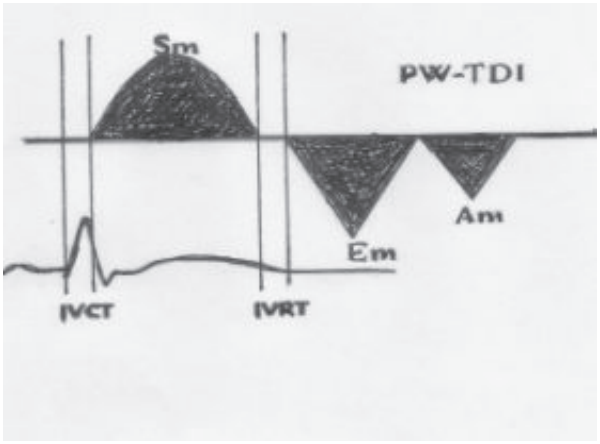

Fig: 2 *This diagram shows myocardial velocity curve by Tissue Doppler Imaging. Sm=systolic velocity. Em=early diastolic velocity, Am= Late diastolic velocity, IVCT=Isovolumetric contraction time, IVRT= Isovolumetric relaxation time 04)*

Assessment of Intraventricular Asynchrony: Intraventricular asynchrony promotes electro-mechanical delays between the walls of the left ventricle, and there are several ways to analyze it through an echocardiography. a) Septal to posterior wall motion delay (SPWMD) :This was measured as the shortest interval between maximum Posterior displacement of septum and maximum anterior displacement of LV posterior wall on M–mode in a parasternal short axis view at papillary muscle level and was considered significant when it was e”130 msec. [12,9]. b) Lateral-to-septal delay (LSD): Spectral pulsed-wave tissue Doppler imaging (PW-TDI) was applied online by placing the sample volume in the middle of the basal portions of the LV septal and lateral walls in an apical four chamber view. Gain and filter settings were adjusted to allow for a clear tissue signal. Myocardial tissue velocities were recorded end-expiratory at a sweep speed of 100 mm/s (Fig-2) and the time to start of the QRS complex to peak systolic velocity (TP) of septal and lateral wall were measured [13] . Each parameter was measured for three consecutive beats & was averaged. Left ventricular asynchrony was defined as a lateral-to-septal delay (LSD)>60 ms, in accordance with the published data from colour TDI [9, 14]. All TDI time intervals were measured by one single observer who was blinded to the patient’s data performed.

Data were expressed as mean±standard deviation for continuous variables and as frequency and percentages for discrete variables. Descriptive statistics were done by mean, standard deviation, multiple responses & Cross table. Chi- square test, ANOVA were done in define groups (by QRS complex).Linear regression analysis were performed to determine the relationship between QRS duration and Interventricular, Intraventricular asynchrony .All statistical analysis were performed using SPSS (Statistical Package for Social Sciences), version 16.0 Level of significance was set at .05 and p-value <0.05 was considered significant.

Results

Among the 103 heart failure patient majority 36(35%) were at the age group between 55-65 years, 25(24.3%) were at the age group between 45-55 years, 23.3% aged more than 65 years and only 3 were aged less than 35 years. Mean age was 57.9±11.9 (range 23-82 years). Majority of them were male (70.9%) and rest 29.1% were female. Male: Female ratio was 2:1

Table-I

Distribution of the subject by age

Age group	Frequency	Percent
<35 years	3	2.9
35-45 years	15	14.6
45-55 years	25	24.3
55-65 years	36	35.0
>65 years	24	23.3
Total	103	100.0

Mean age 57.9±11.9

Table-II

Distribution of the subject by risk factors

Risk factor	Responses	
	N	Percent of Cases
Diabetics	30	32.3%
Hypertension	46	49.5%
Tobacco Smoking	66	71.0%
Dyslipidemia	39	41.9%
Bronchial Asthma	10	10.8%
IHD	21	22.6%
Obesity	19	20.4%
Total	231	248.4%

(**Multiple response observed)

Diabetics was found among the 30(32.3%) patients, 46(49.5%) were hypertensive, 66(71.0%) were tobacco smoker, Dyslipidemia were present among 39(41.9%) patients, 10(10.8%) has been suffered from bronchial asthma, 21(22.6%) had IHD and obesity was common 19(20.4%) patients.

Interventricular asynchrony (IVMD) was significantly lowest in Group-1 (23.65±13.58) compared to Group-II (45.15±26.36) and Group-III (40.92±30.77) (P<0.001)

Intraventricular asynchrony by measuring Septal to post wall motion delay (SPWMD) in msec was also lowest in narrow QRS group (124±43.68) compared to intermediate (133±38.05) and wide QRS (137±39.61) group. Though mean SPWMD were increased in wide & intermediate QRS group, but it was not significant (P>0.05). The magnitude of Lateral-to-septal delay (LSD) were gradually increased among the groups (51.51±42.03vs 62.94±31.71vs 64.11±38.47) but not significantly (P>0.05).

Lateral to Septal delay (LSD) more than 60 ms were found 18(31%) among the group where QRS delay less than 120ms, 9(47.4%) where QRS delay were between 120-150ms and 17(65.4%) where QRS delay more than 150ms.

Among the 47 patient those who have Septal to posterior wall motion delay (SPWMD) (>130ms), 22(37.9%) among the group where QRS delay less than 120ms, 9(47.4%) where QRS delay between 120-150ms and 16(61.5%) where QRS delay more than 150 ms. Interventricular Mechanical delay (IVMD) were found 4(6.9%) with narrow QRS group (<120ms), 12(63.3%) with intermediate group and 17(65.4%) with wide QRS group (>150ms).

Table- III

Comparison of Interventricular & Intraventricular Asynchrony among three groups

Asynchrony	QRS duration			P value
	<120 ms G-I(n=58)	120-150 ms G-II (n=19)	>150ms G-III (n=26)	
Interventricular Asynchrony (IVMD) ms	23.65±13.58	45.15±26.36	40.92±30.77	P=.000^{S}
Intraventricular Asynchrony(SPWMD) ms	124 ±43.68	133± 38.05	137±39.61	P=0.379^{NS}
Intraventricular Asynchrony(LSD) ms	51.51±42.03	62.94±31.71	64.11±38.47	P=0.370^{NS}

Data were analyzed using ANOVA statistics and were presented as Mean±SD.S=significant NS=non significant

Table-IV

Distribution of the subject by different measurement of ventricular conduction delays among three groups

Asynchrony	QRS duration			Total
	<120 msG-I (n=58)	120-150 msG-II (n=19)	>150msG-III (n=26)	
LSD >60 ms	18(31%)	9(47.4%)	17(65.4%)	44
SPWMD>130ms	22(37.9%)	9(47.4%)	16(61.5%)	47
IVMD >40 ms	4(6.9%)	12(63.3%)	17(65.4%)	33

Table-V

Comparison of 2D &M-mode echocardiographic characteristics of patients among three groups.

	QRS duration			
	<120 ms (n=58)	120-150 ms (n=19)	>150ms(n=26)	P value
EF (%)	28.51±4.85	27.73±4.84	26.79±3.91	0.249^{NS}
EDV(ml)	148.50±27.74	163.00±37.28	181.53±27.80	0.000^{S}
ESV(ml)	110.62±23.04	119.94±29.57	136.34±22.50	0.000 ^{S}
LVIDd	66.51±7.63	66.05±6.98	68.50±8.90	0.005 ^{S}
LVIDs	53.29±7.28	53.47±13.87	59.65±8.54	0.012 ^{S}

#Data were analyzed using ANOVA statistics and were presented as Mean ± SD S=significant NS=non significant

2D & M-mode echocardiography findings of patients demonstrate that EDV, ESV, LVIDd & LVIDs were significantly lowest in narrow complex group (QRS<120ms) compared to intermediate and wide QRS (>150ms) groups (p=0.000, p=0.000, p=0.005 and p=0.012 respectively), while ejection fraction was significantly highest in narrow complex group that those in intermediate and wide complex groups (p=0.249)

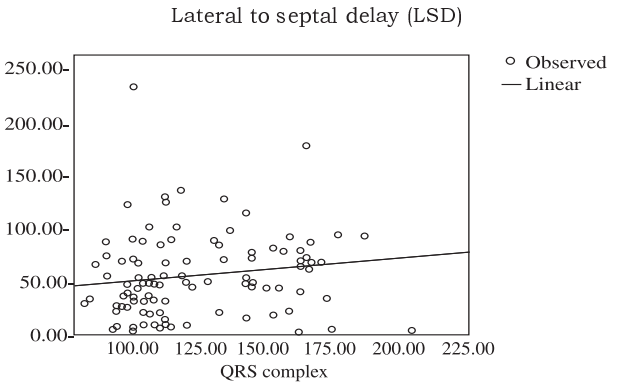

Fig.- 3 *Relationship between QRS duration and Lateral-to-Septal (LDS) delay*

Linear regression demonstrated no relation between QRS duration and lateral-to-septal (LSD) delay among the patients (Y=0.215x+29.62, n=103, r=0.152, p=0.126

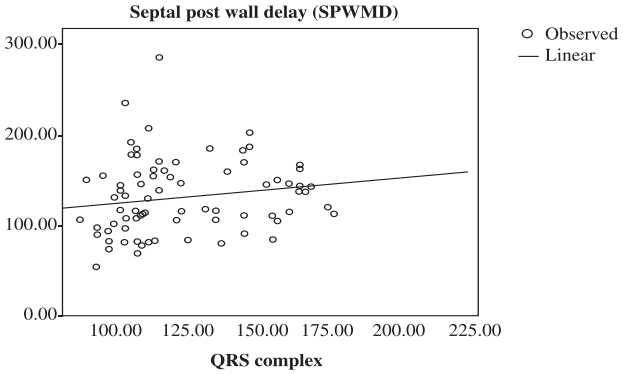

Fig.-4 *Relationship between QRS duration and Septal-post wall motion delay (SPWMD)*

Linear regression demonstrated no relation between QRS duration and septal-to-posterior delay among the patients (Y=0.291x+91.736, n=103, r=0.199, p=0.044)

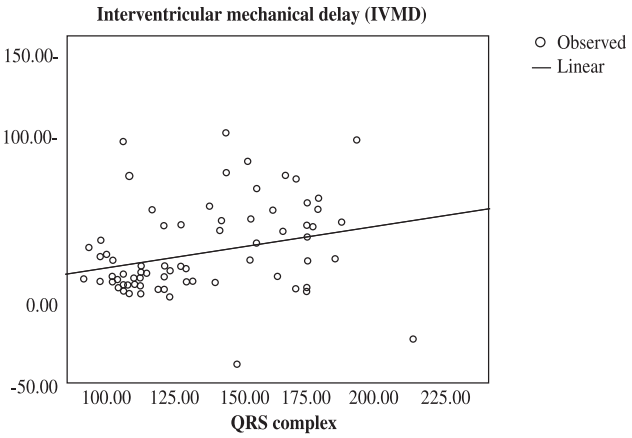

Fig.-5: *Relationship between QRS duration and interventricular mechanical delay (IVMD)*

Linear regression demonstrated very weekly relation between QRS duration and interventricular mechanical delay among the patients (Y=0.314x+7.61, n=103, r=0.372, p=0.000)

Discussion

Among the 103 patients majority of the subjects with systolic dysfunction were older than 50 years and male (70.9%), the mean age was 57.9±11.9 years. it is similar to other study done by Bader et al [10] who found mean ages of heart failure 59 ± 16, most patients were male (86%).In Bangladesh another study by Kabiruzzaman et al described that mean age (54.1 ±15.3) of heart failure is lower in our country than abroad[7].

Smoking was the major risk factor 66(71%), 46(49.5%) patients were hypertensive, 21(22%) patients had previous history of CAD, 30(32.3%) patients were

diabetic & Dyslipidaemia was present about 41.9 % (Table: II). It is similar to other study.

Interventricular asynchrony by measuring interventricular mechanical delay (IVMD) were significantly lowest in Group-1 (23.65±13.58) compared to Group-II (45.15±26.36) and Group-III (40.92±30.77) (P<0.001) (Table-III). So significant increase in IVMD was noted over three groups. Again 65.4% patients of wide QRS(>150 ms) group & 63.3% of intermediate QRS group did not show interventricular asynchrony In addition, a small percentage of patients with narrow QRS duration(<120ms) also showed interventricular asynchrony(6.9%)(Table.IV).

This findings were consistent with that of Ghio (18±20 vs 43±30 vs 59±29,p<.o5) .Ghio also demonstrated 38% patients of wide QRS group & 47.6% of intermediate group failed to show interventricular asynchrony but 11.5% of narrow QRS group showed significant asynchrony[11].

Intraventricular asynchrony by measuring Septal to post wall motion delay (SPWMD) in msec was also lowest in narrow QRS group (124±43.68) compared to intermediate (133±38.05) and wide QRS (137±39.61) group. Though mean SPWMD were increased in wide & intermediate QRS group, but it was not significant (P>.o5) It is similar to study done in India by Kumar &Goel[15].

The magnitude of Lateral-to-septal delay (LSD) was gradually increased among the groups (51.51±42.03vs 62.94±31.71vs 64.11±38.47) but not significantly. (P>0.05) using the cut off value 60 ms, this study found 65.4% patients of wide QRS (>150ms) group and 47.4% of intermediate group had significant asynchrony. Majority of patients (69%) of narrow QRS complex did not exhibit asynchrony, interestingly 31% showed significant asynchrony. (Table-V) These findings had similarities with the study by Bleeker et al [16].

Another study by Bader et al, illustrated that the presence of intra-LV (but not inter-V) asynchrony was identified as an independent predictor of severe cardiac events (hazard ratio 3.39, p < 0.0001), independent of the LVEF and QRS width and also showed that patients with a QRS width <120 ms (55%; n = 57),56% presented with major intra-LV asynchrony and 12% with inter-Vasynchrony[10].

Mean difference between ejection fraction (EF) and QRS duration has no significant value (P=0.249).Left ventricular end diastolic volume (EDV) and end systolic Volume were increased in parallel to QRS duration (P<0.001(Table-V).LVIDd & LVIDs were also significantly increased in wide (>150ms) & intermediate QRS(120-150ms) compared to narrow QRS(<120ms) group(P=0.005 P=0.012) These finding had similarities with the study of Bleeker et al [16].

In this study, among the patients of intraventricuar asynchrony, Linear regression failed to demonstrate any relation between QRS duration and Lateral-to-septal delay(Y=0.215x+29.62, n=103, r=0.152, p=0.126) (Fig-3) Bleeker et al, also showed no relation between them.(r=0.18,NS)

Also no significant relation existed between QRS duration and septal-to-posterior wall delay. (Y=0.291x+91.736, n=103, r=0.199, p=0.044)(Fig-4) But among the patients of interventricular asynchrony, though widely scattered data Linear regression demonstrated weak relation between QRS duration IVMD (Y=0.314x+7.61, n=103, r=0.372, p=0.000) (Fig-5) which was very much similar to the study done by Zakhama et al, (r=0.35 p=0.4)[17].

So, the main result of the present study is the poor relationship between QRS duration and cardiac asynchrony observed by conventional and more sophisticated echocardiographic techniques. Even though it was affirmed by Rouleau et al, who showed a good correlation between IVMD and QRS width (r=0.86, p<0.01), [18] it failed to show this correlation in this series, this same result had been reported by Ghio in a larger series of dilated cardiomyopathy: despite a significant correlation between interventricular delay and QRS duration (r=0.66, p<01), a wide scattering of the data around the identity line was observed[11]. This data suggests that, the QRS width appears to be poorly correlated with the presence of inter-V and intra-LV electromechanical asynchrony.

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