Echocardiographic Assessment of Ventricular Dyssynchrony in Left Ventricular Systolic Dysfunction and Valvular Heart Disease

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Abstract

Background- Mechanical dyssynchrony is common in patients with heart failure and its presence predicts patient response to cardiac resynchronization therapy (CRT).The quantification of left ventricular dyssynchrony using tissue Doppler imaging (TDI) may improve the selection of these patients. We aimed to evaluate the prevalence of dyssynchrony in patients with heart failure and valvular heart disease with either normal or prolonged QRS durations.

Methods- Patients with left ventricular (LV) systolic dysfunction and significant organic valvular heart disease were evaluated. Using conventional and tissue Doppler echocardiography, an interventricular mechanical delay >40 ms was defined as significant interventricular dyssynchrony. Intraventricular dyssynchrony was evaluated using the calculation of the septal-to-lateral wall delay, the SD of the time from the Q wave to the peak systolic wave of 6 basal and 6 mid segments, and the maximum difference in the time from the Q wave to the peak systolic wave of all 12 segments.

Results- Forty-four patients (22 female, mean age 47 ± 15.2 years) were evaluated. Interventricular dyssynchrony was present in 12 (27%) patients. Intraventricular dyssynchrony was present in 17 (39%) to 19 (43%) patients, depending on the method used. Interventricular and intraventricular mechanical dyssynchrony had a significant association with LV volume and QRS duration (independent of the type of valvular heart disease). We found almost perfect agreement between maximum difference and total dyssynchrony index (kappa = 0.91), and the overall agreement among septum-to-lateral delay, maximum difference, and total dyssynchrony index was good (kappa = 0.72).

Conclusion- Although ventricular dyssynchrony in patients with valvular heart disease and LV dysfunction is not highly prevalent, it has a significant association with QRS duration and LV size ***(Iranian Heart Journal 2009; 10 (2):5-14).***

Received May 8, 2008; Accepted for publication May 21, 2009.

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Cardiac resynchronization therapy (CRT) is increasingly used in patients with heart failure (HF) and left ventricular (LV) systolic dysfunction.[1–4]

CRT results in significant improvements in functional and clinical outcomes in a majority of patients. These benefits are observed regardless of an ischemic or non-ischemic cause of HF.[5-11]

The only ventricular dyssynchrony marker to select patients for CRT included in HF guidelines was the presence of a wide QRS,[13] but the electrocardiographic approach might not be sensitive enough for reliable identification of all patients with correctable mechanical dyssynchrony. Echocardiographic and Doppler studies provide non-invasive insights into cardiac function and regional dyssynchrony and may help to improve dyssynchrony detection. One of the most frequently used modalities for this purpose is tissue Doppler imaging (TDI). These techniques have the advantages of being non-invasive, easy, and inexpensive. DTI measurements of LV intraventricular dyssynchrony can be used to predict hemodynamic response after CRT.[12] A few studies have assessed the potential effect of biventricular pacing in patients with HF and significant primary valvular heart disease. Our literature review did not yield any study on mechanical dyssynchrony as assessed by echocardiography, including TDI, in these patients.

The aim of this study was : (1) to determine the prevalence of interventricular and intraventricular dyssynchrony by Doppler echocardiography in consecutive patients with LV systolic dysfunction (with or without HF symptoms) and valvular heart disease by using different Doppler echocardiographic modalities, (2) to determine the association of LV size and QRS duration with left ventricular dyssynchrony in patients with LV systolic dysfunction and various form of valvular heart disease, and (3) to assess the agreement among different Doppler echocardiographic methods to evaluate intraventricular cardiac dyssynchrony.

Methods

Patients

In all, 44 consecutive patients were referred for echocardiographic studies. All of them had an LV ejection fraction (EF) which was assessed by Simpson's method of equal or less than 35%. Exclusion criteria were: previous myocardial infarction or significant stenosis in coronary angiography for the exclusion of ischemic cardiomyopathy, patients with non-ischemic dilated cardiomyopathy, patients with prostheses and early after valve surgery with stunned myocardium, patients on CRT or paced, atrial fibrillation with rapid ventricular response, and patients with functional MR. All the patients' clinical charts were used to obtain the clinical variables.

A recent electrocardiogram was used to determine the electrocardiographic variables.

Echocardiographic determination of interventricular dyssynchrony

Interventricular dyssynchrony was defined as a difference between the time from Q wave to the start of RV ejection and the time from Q wave to the start of LV ejection. A value greater than 40 milliseconds was considered abnormal.

Echocardiography

After a standard echocardiographic study, eligible patients for inclusion were informed about the study.

Echocardiography was performed using a Vivid 7 (GE VingMed, Milwaukee, WI) equipped with a 2.5-MHz phased-array transducer.

DTI was performed from 2-chamber, 4-chamber, and apical long axis views with an optimal Doppler insonation angle (Fig. 1).
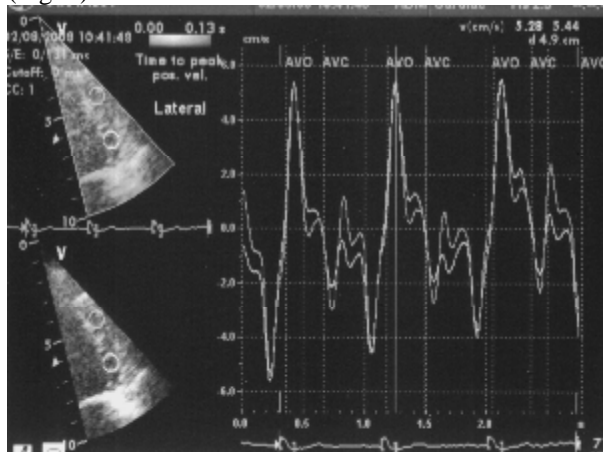
Fig. 1. Assessment of left ventricular intraventricular dyssynchrony by Doppler tissue imaging showing no difference in time to peak systolic velocity in base and mid of lateral wall. AVC, aortic valve closure; AVO, aortic valve opening

LV volume and EF were evaluated by Simpson's method and graded according to the ASE guidelines. The images were acquired with a sweep speed of 100 cm/s, with gains and filters optimized.

TDI measurements were sampled from 3 cardiac cycles at each location and the results were averaged. Time from Q wave to peak systolic velocity of the 12 LV segments, basal and mid of anterior, inferior, lateral, septal, posterior, and anteroseptal were assessed by offline DTI.

Echocardiographic determination of intraventricular dyssynchrony

Intraventricular dyssynchrony was evaluated using 3 different methods.

First, basal septum to basal lateral mechanical delay difference longer than 60 milliseconds was considered an intraventricular dyssynchrony marker.[14]

Second, maximum difference in time to peak velocity of all 12 segments was compared, and intraventricular dyssynchrony was established when a maximum difference greater than 100 milliseconds was present.[14]

Third, intraventricular dyssynchrony assessment using the SD of the time from the Q wave to the peak of the systolic wave of all 12 segments (total asynchrony index) established intraventricular dyssynchrony when the total asynchrony index was greater than 32.6.[14]

Statistical Analysis

The data were classified as mean ± standard deviation (SD) for intervals and frequency (relative frequency) for the categorical variables. Student's t, Mann Whitney U, Pearson's chi-square, and Fisher's exact tests were used to compare the different types of data between the two groups. McNemar and Cochrane's Q tests were also used to compare the results among different asynchrony indices.

Kappa statistics were calculated to show the agreements. Logistic regression models were fitted to determine the adjusted associations between each of the dyssynchrony indices (as dependent variables) and other independent factors. Stata[TM] 8 for Windows (Stata Corporation, Texas, USA) was used for statistical analysis.

Inter- and intra-observer variability

All the echocardiographic examinations were performed by one board-certificated echocardiologist. For measuring intra- observer reliability, 10 records were randomly selected and the echocardiologist, who was blinded about the identity of the patients, re-evaluated the films to determine the four indices of dyssynchrony.

Kappa statistics were calculated to investigate the agreement between the two sets of data. No difference was observed in the determination of dyssynchrony based on SLD and IVD on the first and second times, and then kappa ± SE was calculated as 1.00 ± 0.32.

According to TAI, dyssynchrony was reported in 7 patients; but on the second time, dyssynchrony was diagnosed in 8 patients. Kappa ± SE was calculated as 0.74 ± 0.31. Also, according to MD, dyssynchrony existed in 6 patients, whereas it existed in 7 patients on the second time and kappa ± SE was calculated as 0.78 ± 0.31 in this case. The agreement between the two evaluations can be considered as good to almost perfect.

Results

Baseline data

In total, 44 patients (22 female, mean age 47 ± 15.2 years, range 16 to 76 years) were included. Mean LVEF was 27 ± 7.5%. Among the participants, 17 (0.39) had severe, 8 (0.18) had moderate, and 12 (0.27) had mild LV enlargement. In 7 (0.16) cases, LV volumes were within normal range.

Among the patients, QRS complexes were narrow (<120 milliseconds) in 19 (42.2%) patients, prolonged (>120 milliseconds) in 18 (41%), and 120 milliseconds in 7 (15.6%). Of the 44 participants, we found significant organic mitral regurgitation (MR) in 15 (0.34), mitral stenosis (MS) in 26 (0.59), aortic insufficiency (AI) in 12 (0.27), and aortic stenosis (AS) in 9 (0.21) cases. Seventeen (0.39) patients had mitral and 8 patients had aortic valve prostheses.

Dyssynchrony indices and their agreements

The mean values for dyssynchrony indices were: 28 ± 23.2 msec for interventricular delay, 52 ± 30.9 msec for septum-to-lateral delay, 85 ± 36.7 msec for maximum difference, and 33.1 ± 14.6 msec for total dyssynchrony indexes. Dyssynchrony was observed in 12 (0.27) patients according to inter-ventricular delay, 17 (0.39) patients according to

septum-to-lateral delay, 19 (0.43) patients according to maximum difference, and 19 (0.43) patients according to total dyssynchrony index. There was no significant difference in the diagnosis of dyssynchrony among the 3 intra-ventricular indices of asynchrony (Cochran's Q = 0.89, df = 2, P-value = 0.64). The agreement between the maximum difference and total asynchrony index was almost perfect (kappa = 0.91). Computing multi-rater kappa statistics showed that the overall agreement among septum-to-lateral delay, maximum difference, and total asynchrony index was good (kappa = 0.72). The results of the intraventricular dyssynchrony indices were compared to inter-ventricular delay. The agreement was poor- good (kappa = 0.27).

Table I. Associations between cardiac asynchrony according to total asynchrony index and other determinants*

	Asynchrony (TAI)		P value	OR [95% CI]
	Present (n = 19)	Absent (n = 25)		
Age *years*	51 ± 15.1	44 ± 14.8	0.11	-
Sex			0.13	2.56 [0.75 – 8.78]
Male (n = 22)	12 (0.63)	10 (0.40)		
Female (n = 22)	7 (0.37)	15 (0.60)		
QRS Wave Pattern			0.17	2.36 [0.69 – 8.06]
Wide (n = 18)	10 (0.53)	8 (0.32)		
Narrow (n = 26)	9 (0.47)	17 (0.68)		
LVEF %	25 ± 8.1	28 ± 6.9	0.20	-
LV Enlargement			0.03	-
Severe (n = 17)	11 (0.58)	6 (0.24)		
Moderate (n = 8)	1 (0.05)	7 (0.28)		
Mild (n = 12)	7 (0.37)	5 (0.20)		
Normal (n =7)	0	7 (0.28)		
Mitral Stenosis			0.45	0.63 [0.19 – 2.11]
Yes (n = 26)	10 (0.53)	16 (0.64)		
No (n = 18)	9 (0.47)	9 (0.36)		
Mitral Regurgitation			0.76	0.82 [0.23 – 2.91]
Yes (n = 15)	6 (0.32)	9 (0.36)		
No (n = 29)	13 (0.68)	16 (0.64)		
Aortic Stenosis			0.93	1.07 [0.24 – 4.67]
Yes (n = 9)	4 (0.21)	5 (0.20)		
No (n = 35)	15 (0.79)	20 (0.80)		
Aortic Insufficiency			0.05	3.82 [0.94–15.56]
Yes (n = 12)	8 (0.42)	4 (0.16)		
No (n = 32)	11 (0.58)	21 (0.84)		
Mitral Valve Prosthesis			0.83	0.88 [0.26 – 2.99]
Yes (n = 17)	7 (0.37)	10 (0.40)		
No (n = 27)	12 (0.63)	15 (0.60)		
Aortic Valve Prosthesis			0.05	5.31 [0.93–30.20]
Yes (n = 8)	6 (0.32)	2 (0.08)		
No (n = 36)	13 (0.68)	23 (0.92)		
Mitral Valve Prosthesis due to MS			0.05	0.21 [0.04 – 1.12]
Yes (n = 11)	2 (0.11)	9 (0.36)		
No (n = 33)	17 (0.89)	16 (0.64)		

LVEF: left ventricular ejection fraction; OR: odds ratio; CI: confidence interval* Parentheses represent *relative frequenc*y of data in each column. Numbers after ± represent *standard deviations.*

Determinants of total asynchrony index

The relationships between TAI and other variables are presented in Table I. No association was found between TAI and age, sex, and QRS wave pattern. Among patients with asynchrony, 10 (0.53) had wide and 9 (0.47) had narrow QRS wave patterns. On the other hand, in patients with negative findings, 8 (0.32) had wide and 17 (0.68) had normal

patterns (P-value = 0.17). LV size had a significant relationship with asynchrony (P- value = 0.03). Severe enlargement of LV was associated with asynchrony (Fig 2).
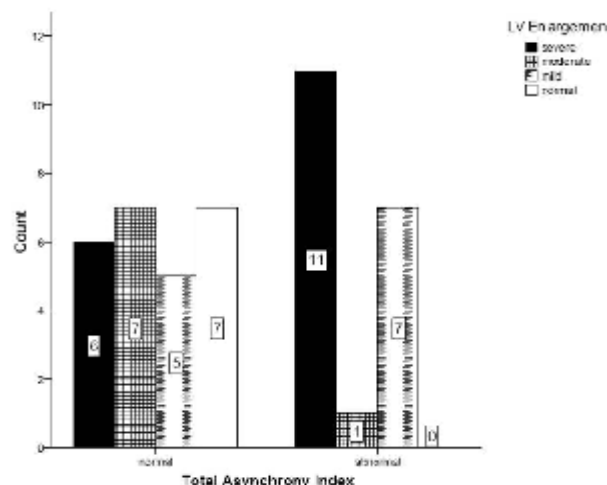

Fig. 2 Total Asynchrony Index, in patients with valvular heart disease and various degrees of QRS duration.

Mild and moderate enlargement did not have any associations with asynchrony (Table I). A logistic regression model was fitted and revealed that after adjustment for all the above-mentioned variables, none of the valvular heart diseases had a significant association with TAI.

Determinants of septum-to-lateral delay (SLD)
It was observed that only QRS duration, aortic stenosis (AS), and mitral valve prosthesis due to MS were related to this index of asynchrony. Among patients with asynchrony, 10 (0.59) had wide and 7 (0.41) had narrow QRS wave patterns. In patients with negative findings, 8 (0.30) had wide and 19 (0.70) had normal patterns (P-value = 0.05; OR = 1.05 [CI 95%: 0.95–12.05]). No association was observed between LV size and asynchrony (P-value =0.13, Table II). The prevalence of AS was greater in patients with asynchrony (P-value =0.05; OR =4.36 [CI95%: 0.92–20.47]). Similar to TAI, the asynchrony was associated with the less number of MVR (MS), OR = 0.11 [CI95%: 0.01 – 0.93]; P- value =0.02).
Other factors did not show any relationship with SLD (Table II).

Table II. Associations between cardiac dyssynchrony according to septum–to-lateral asynchrony index (SLA) and other determinants*

	Asynchrony (SLA)		P value	OR [95% CI]
	Present (n = 17)	Absent (n = 27)		
Age *years*	51 ± 14.9	45 ± 15.1	0.18	-
Sex			0.35	1.79 [0.52 – 6.10]
Male (n = 22)	10 (0.59)	12 (0.44)		
Female (n = 22)	7 (0.41)	15 (0.56)		
QRS Wave Pattern			0.05	1.05 [0.95–12.05]
Wide (n = 18)	10 (0.59)	8 (0.30)		
Narrow (n = 26)	7 (0.41)	19 (0.70)		
LVEF %	26 ± 8.1	28 ± 7.1	0.35	-
LV Enlargement			0.13	-
Severe (n = 17)	9 (0.53)	8 (0.30)		
Moderate (n = 8)	1 (0.06)	7 (0.26)		
Mild (n = 12)	7 (0.41)	5 (0.18)		
Normal (n =7)	0	7 (0.26)		
Mitral Stenosis			0.20	0.44 [0.13 – 1.54]
Yes (n = 26)	8 (0.47)	18 (0.67)		
No (n = 18)	9 (0.53)	9 (0.33)		
Mitral Regurgitation			0.89	1.10 [0.30 – 3.91]
Yes (n = 15)	6 (0.35)	9 (0.33)		

No (n = 29)	11 (0.65)	18 (0.67)		
Aortic Stenosis			0.05	4.36 [0.92–20.47]
Yes (n = 9)	6 (0.35)	3 (0.11)		
No (n = 35)	11 (0.65)	24 (0.89)		
Aortic Insufficiency			0.10	3.10 [0.78–12.12]
Yes (n = 12)	7 (0.41)	5 (0.18)		
No (n = 32)	10 (0.59)	22 (0.82)		
Mitral Valve Prosthesis			0.72	0.79 [0.23 – 2.79]
Yes (n = 17)	6 (0.35)	11 (0.41)		
No (n = 27)	11 (0.65)	16 (0.59)		
Aortic Valve Prosthesis			0.13	3.33 [0.68–16.35]
Yes (n = 8)	5 (0.29)	3 (0.11)		
No (n = 36)	12 (0.71)	24 (0.89)		
Mitral valve prosthesis due to MS			0.02	0.11 [0.01 – 0.93]
Yes (n = 11)	1 (0.06)	10 (0.37)		
No (n = 33)	16 (0.94)	17 (0.63)		

LVEF: left ventricular ejection fraction; OR: odds ratio; CI: confidence interval * Parentheses represent *relative frequenc*y of data in each column. Numbers after ± represent *standard deviations.*

In the multivariate analysis, a logistic regression model was fitted. All the factors failed to show a significant association with SLD after adjustment.

Determinants of maximum difference (MD)
The data are presented in Table III. Asynchrony based on this index was related to LV size and QRS duration.
Among patients with asynchrony, 10 (0.59) had wide and 7 (0.41) had narrow QRS wave patterns. In patients with negative findings, 8 (0.30) had wide and 19 (0.70) had normal patterns (P-value =0.05; OR =1.05 [CI 95%: 0.95–12.05]). Results in Table III show that similar to TAI, severe enlargement of the LV was associated with asynchrony and normal LV size was related to normal cardiac function (P-value =0.02).
No significant relationships were observed between MD and other factors like age, sex, and valvular diseases and prosthesis.

Determinants of interventricular delay (IVD)
No relationship was found between IVD and age, sex, valvular diseases and prosthesis (Table IV).
Among patients with dyssynchrony, 10 (0.83) had wide and 2 (0.17) had narrow QRS wave patterns. In patients with normal hearts, 8 (0.25) had wide and 24 (0.75) had normal patterns. This result showed that wide QRS pattern had a significant association with IVD (P-value <0.001; OR = 14.93 [CI 95%: 2.70–83.3]). Low precision of the result (wide CI 95%) restricted its usage.
It was shown that LV size had a positive relationship with IVD (P-value = 0.002) (Fig 3).

Table III. Associations between cardiac asynchrony according to maximum difference (MD) and other determinants *

LVEF: Left Ventricular Ejection Fraction; OR: Odds Ratio; CI: Confidence Interval

	Asynchrony (MD)		P value	OR [95% CI]
	Present (n = 19)	Absent (n = 25)		
Age *years*	52 ±14.9	44 ± 14.8	0.09	
Sex			0.36	1.75 [0.52 – 5.24]
Male (n = 22)	11(0.58)	11 (0.44)		
Female (n = 22)	8 (0.42)	14 (0.56)		
QRS Wave Pattern			0.17	2.36 [0.69 – 8.06]
Wide (n = 18)	10 (0.53)	8 (0.32)		
Narrow (n = 26)	9 (0.47)	17 (0.68)		-
LVEF %	25 ± 8.1	28 ± 6.9	0.20	
LV Enlargement			0.02	-
Severe (n = 17)	11(0.58)	6 (0.24)		
Moderate (n = 8)	2 (0.10)	6 (0.24)		
Mild (n = 12)	6 (0.32)	6 (0.24)		
Normal Size (n =7)	0	7 (0.28)		
Mitral Stenosis			0.45	0.63 [0.19 – 2.11]
Yes (n = 26)	10(0.53)	16 (0.64)		
No (n = 18)	9 (0.47)	9 (0.36)		
Mitral Regurgitation			0.74	1.24 [0.35 – 4.35]
Yes (n = 15)	7 (0.37)	8 (0.32)		
No (n = 29)	12(0.63)	17 (0.68)		
Aortic Stenosis			0.93	1.07 [0.24 – 4.67]
Yes (n = 9)	4 (0.21)	5 (0.20)		
No (n = 35)	15(0.79)	20 (0.80)		
Aortic Insufficiency			0.21	2.30 [0.60–9.02]
Yes (n = 12)	7 (0.37)	5 (0.20)		
No (n = 32)	12(0.63)	20 (0.80)		
Mitral Valve Prosthesis			0.40	0.59 [0.17 – 2.05]
Yes (n = 17)	6 (0.32)	11 (0.44)		
No (n = 27)	13(0.68)	14 (0.56)		
Aortic Valve Prosthesis			0.20	2.62 [0.54–12.72]
Yes (n = 8)	5 (0.26)	3 (0.12)		
No (n = 36)	14(0.74)	12 (0.88)		
Mitral valve prosthesis due to MS			0.05	0.21 [0.04 – 1.12]
Yes (n = 11)	2 (0.11)	9 (0.36)		
No (n = 33)	17(0.89)	16 (0.64)		

	Asynchrony (IVD)		P value	OR [95% CI]
	Present (n = 12)	Absent (n = 32)		
Age *years*	51 ± 17.7	45 ± 14.1	0.27	-
Sex			0.18	0.39 [0.40 – 1.56]
Male (n = 22)	4 (0.33)	18 (0.56)		
Female (n = 22)	8 (0.67)	14 (0.44)		
QRS Wave Pattern			<0.001	14.93[2.70–83.3]
Wide (n = 18)	10 (0.83)	8 (0.25)		
Narrow (n = 26)	2 (0.17)	24 (0.75)		
LVEF %	23 ± 6.9	29 ± 7.1	0.02	-
LV Size			0.002	-
Severe enlargement (n = 17)	9 (0.75)	8 (0.25)		
Moderate enlargement (n = 8)	2 (0.17)	6 (0.19)		
Mild enlargement (n = 12)	1 (0.08)	11(0.34)		
Normal Size (n =7)	0	7 (0.22)		
Mitral Stenosis			0.45	0.60 [0.16 – 2.29]
Yes (n = 26)	6 (0.50)	20 (0.63)		
No (n = 18)	6 (0.50)	12 (0.37)		
Mitral Regurgitation			0.95	0.96 [0.23 – 3.89]
Yes (n = 15)	4 (0.33)	11 (0.34)		
No (n = 29)	8 (0.67)	21 (0.66)		
Aortic Stenosis			0.22	0.27 [0.33 – 2.46]
Yes (n = 9)	1 (0.08)	8 (0.25)		
No (n = 35)	11 (0.92)	24 (0.75)		
Aortic Insufficiency			0.58	1.50 [0.36–6.35]
Yes (n = 12)	4 (0.33)	8 (0.25)		
No (n = 32)	8 (0.67)	24 (0.75)		
Mitral Valve Prosthesis			0.80	1.19 [0.31 – 4.60]
Yes (n = 17)	5 (0.42)	12 (0.38)		
No (n = 27)	7 (0.58)	20 (0.62)		
Aortic Valve Prosthesis			0.87	0.87 [0.15 – 5.03]
Yes (n = 8)	2 (0.17)	6 (0.19)		
No (n = 36)	10 (0.83)	26 (0.81)		
Mitral valve prosthesis due to MS			> 0.99	1.00 [0.22 – 4.63]
Yes (n = 11)	3 (0.25)	8 (0.25)		
No (n = 33)	9 (0.75)	25 (0.75)		

* Parentheses represent *relative frequency* of data in each column.
Numbers after ± represent *standard deviations*

Table IV. Associations between cardiac asynchrony according to inter-ventricular delay (IVD) and other determinants *

LVEF: left ventricular ejection fraction; OR: odds ratio; CI: confidence interval

* Parentheses represent *relative frequency* of data in each column. Numbers after ± represent *standard deviations.*

But unlike other indices, only severe enlargement was associated with asynchrony and the difference among other degrees of enlargement or normality between the two groups was not important (Table IV).
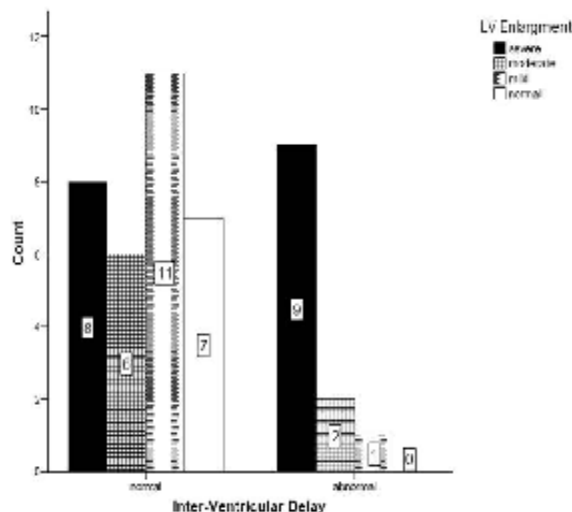

Fig. 3. Graph showing distribution of interventricular delay.

Discussion

Our study describes the prevalence of interventricular and intraventricular dyssynchrony in a series of consecutive patients with valvular heart disease and significantly decreased LV systolic function. Until now, according to our literature review there has been no other study to evaluate the presence of cardiac dyssynchrony in such patients.

We found 27% interventricular dyssynchrony, which is not highly prevalent compared to the previously reported interventricular dyssynchrony in patients with ischemic and non-ischemic heart failure (26% in those patients with normal QRS complexes and 55% in those patients with prolonged QRS complexes).[15] Our results were not completely comparable with previous studies because the patient selection and study design were different. Interventricular dyssynchrony had a significant association with QRS duration and LV enlargement.

Intraventricular dyssynchrony was present in 39% to 43% of our patients, depending on the method used. Perez de Isla et al. found a wide range of variability in the prevalence of intraventricular dyssynchrony irrespective of QRS duration. They reported a prevalence of intraventricular dyssynchrony between 20.8% and 72.8% for patients with narrow QRS and between 26.2% and 79.6% for patients with prolonged QRS and suggested that this variability was dependent on the method and criteria used to establish the dyssynchrony.

In other studies, intraventricular dyssynchrony in patients with ischemic and non-ischemic heart failure ranges between 40% and 75%, based on QRS duration.[15-18]

Our intraventricular dyssynchrony prevalence is at the lower range of all studies, and more studies are needed to evaluate the prevalence of dyssynchrony by QRS complex and echocardiography methods to prove which one is a better predictor of acute hemodynamic,[19] clinical,[20] and echocardiographic[21-24] response in patients undergoing biventricular pacing. We found a significant positive association with QRS width and intraventricular dyssynchrony (by septum to lateral delay and maximum difference methods).

Intraventricular dyssynchrony by TAI and MD had a significant association with LV size. Bader et al. reported 56% intraventricular dyssynchrony in patients with QRS width <120 milliseconds with no significant association between the width of the QRS complex and inter or intraventricular dyssynchrony.[18]

The Perez de Isla study showed enormous discrepancies among different methods, but we found almost perfect agreement between maximum difference and total dyssynchrony index (kappa=0.91), and the overall agreement among septum-to-lateral delay, maximum difference and total dyssynchrony index was good (kappa = 0.72)[16]

In our study, there was no significant association between interventricular and intraventricular dyssynchrony and various types of valvular heart disease, but additional studies are needed in this specific group of patients.

Study limitations

We had a limited number of patients with valvular heart disease and LV systolic dysfunction, and we did not determine the cause and effect between these two parameters. The presence of ventricular dyssynchrony is a determinant of CRT responders; and until now, definite parameters to detect those patients who will benefit from

this treatment have remained unknown. The lack of an echocardiographic gold standard is a limitation in all dyssynchrony evaluation studies.

Conclusion

This study indicates that ventricular dyssynchrony in patients with valvular heart disease and LV dysfunction is not highly prevalent but has independent association with QRS duration and LV enlargement and these two parameters can predict a higher prevalence of inter- and intraventricular dyssynchrony.

References

1. Cazeau S, Leclercq C, Lavergne T, Walker S, Varma C, Luide C, Garrigue S, Kappenberger L, Haywood G, Santini M, Bailleul C, Daubert J, for the Multisite Stimulation in Cardiomyopathies (MUSTIC) Study Investigators. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. N Engl J Med 2001; 344: 873– 880.

2. Abraham WT, Fisher WG, Smith AL, DeLurgio DB, Leon AR, Loh E, Kocovic DZ, Packer M, Clavell AL, Hayes DL, Ellestad M, Messenger J. Cardiac resynchronization in chronic heart failure: Multicenter InSync Randomized Clinical Evaluation (MIRACLE). N Engl J Med 2002; 346: 1845–1853.

3. Leclercq C, Hare JM. Ventricular resynchronization: current state of the art. Circulation 2004; 109: 296 –299.

4. Cleland JGF, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L, for the Cardiac Resynchronization-Heart Failure (CARE-HF) Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med 2005; 352: 1539 –1549.

5. Waggoner AD, Agler, DA, Adams DB. Cardiac resynchronization therapy and the emerging role of echocardiography (part 1): Indications and results from current studies. J Am Soc Echocardiogr 2007; 20: 70-75.

6. Molhoek SG, Bax JJ, Bleeker GB, Boersma E, Erven LV, Steendijk P et al.Comparison of response to cardiac resynchronization therapy in patients with sinus rhythm versus chronic atrial fibrillation *Am J Card 2004, 94(12), 1506-1509.*

7. Pitzalis MV, Iacoviello M, Romito R, Massari F, Rizzon B, Luzzi G, et al. Cardiac resynchronization therapy tailored by echocardiographic evaluation of ventricular dyssynchrony. J Am Coll Cardiol 2002; 40: 1615-22.

8. Bax JJ, Ansalone G, Breithardt OA, Derumeaux G, Leclercq C, Schalij MJ, et al. Echocardiographic evaluation of cardiac resynchronization therapy: ready for routine clinical use? A critical appraisal. J Am Coll Cardiol 2004; 44: 1-9.

9. Kass DA. Predicting cardiac resynchronization response by QRS duration: the long and short of it. J Am Coll Cardiol 2003; 42: 2125-7.

10. Leclercq C, Faris O, Tunin R, Johnson J, Kato R, Evans F,et al. Systolic improvement and mechanical resynchronization does not require electrical synchrony in the dilated failing heart with left bundle-branch block. Circulation 2002; 106: 1760-3.

11. Perez de Isla L, Florit J, Garcia-Fernandez MA, Evangelista A, Zamorano J. Prevalence of echocardiographically detected ventricular dyssynchrony in patients with left ventricular systolic dysfunction. J Am Soc Echocardiogr 2005; 18: 850-859.

12. Sogaard P, MD, Egeblad H, MD, Kim W. Y, MD, Jensen HK, MD,Pedersen AK, MD, Kristensen B, MD, et al. Tissue doppler imaging predicts improved systolic performance and reversed left ventricular remodeling during long-term cardiac resynchronization therapy, J Am Coll Cardiol, 2002; 40:723-730.

13. Yu CM, Chau E, Sanderson JEl: Tissue Doppler echocardiographic evidence of reverse remodeling and improved synchronicity by simultaneously delaying regional contraction after biventricular pacing therapy in heart failure. Circulation 2002; 105: 438-445.

14. Yu C-M, Lin H, Zhang Q, Sanderson JE. High prevalence of left ventricular systolic and diastolic asynchrony in patients with congestive heart failure and normal QRS duration. Heart 2003; 89: 54-60.

15. Ghio S, Conctantin C, Klersy C, et al. Interventricular and intraventricular dyssynchrony are common in heart failure patients, regardless of QRS duration. Eur Heart J 2004; 25: 571-578.

16. Ghio S, Constantin C, C Klersy, Serio A, Fontana A, Campana C **et al.** Interventricular and intraventricular dyssynchrony are common in heart failure patients, regardless of QRS duration**,** European Heart Journal 2004 25(7):571-578.

17. Ansalone G, Giannantoni P, Ricci R, Trambaiolo P, Laurenti A, Fedele F. Doppler myocardial imaging in patients with heart failure receiving biventricular pacing treatment. Am Heart J 2001; 142: 881-96.

18. Sogaard P, Kim WY, Jensen HK, Mortensen P, Pedersen AK, Kristensen BO, et al. Impact of acute biventricular pacing on left ventricular performance and volumes in patients with severe heart failure: a tissue Doppler and three-dimensional echocardiographic study. Cardiology 2001; 95: 173-82.

19. Achilli A, Sassara M, Ficili S, Pontiollo D, Alessi C. Long-term effectiveness of cardiac resynchronization therapy in patients with refractory heart failure and ''narrow" QRS. J Am Coll Cardiol 2003; 42: 2117-2124.

20. Turner MS, Bleasdale RA, Mumford CE, Frenneaux MP, Morris-Thurgood JA. Left ventricular pacing improves hemodynamic variables in patients with heart failure with a normal QRS duration. Heart 2004; 90: 502-505.
21. Pai RG, Kanwaljit SG. Amplitudes, durations, and timings of apically directed left ventricular myocardial velocities: II. Systolic and diastolic dyssynchrony in patients with left ventricular hypertrophy. J Am Soc Echocardiogr 1998; 11: 112-8.