Original Article

# Assessment of Left Ventricular Dyssynchrony in Heart Failure Patients Regarding Underlying Etiology and QRS Duration

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## Abstract

***Background:*** *Left ventricular (LV) dyssynchrony is a prevalent feature in heart failure (HF) patients. The current study aimed to evaluate the prevalence of inter and intraventricular dyssynchrony in HF patients with regard to the QRS duration and etiology.*

***Methods:*** *The available data on the tissue Doppler imaging (TDI) of 230 patients with refractory HF were analyzed. The patients were divided into three groups according to the QRS duration: QRS duration < 120 ms; 120-150 ms; and ≥ 150 ms and the patients were re-categorized into two subgroups depending on the underlying etiology: ischemic cardiomyopathy (ICM) or dilated cardiomyopathy (DCM). The time-to-peak myocardial sustained systolic velocity (Ts) in six basal and six middle segments of the LV was measured manually using the velocity curves from TDI. LV dyssynchrony was defined as interventricular mechanical delay ≥ 40 ms and tissue Doppler velocity all segments delay ≥ 105 ms; standard deviation (SD) of all segments ≥ 34.4 ms; basal segments delay ≥ 78 ms; SD of basal segments ≥ 34.5 ms; and opposing wall delay ≥ 65 ms.*

***Results:*** *After adjustment for the possible confounders, interventricular dyssynchrony was more prevalent in the patients with QRS duration ≥ 150 ms than in those with QRS duration 120-150 ms and < 120 ms. The patients with DCM also had a higher percentage of interventricular dyssynchrony than those with ICM in the wide QRS groups. Turning to the intraventricular dyssynchrony indices, the patients with QRS duration ≥ 150 ms and 120-150 ms revealed a significantly greater delay between Ts at the basal and all segments than did those with QRS duration < 120 ms, while etiology did not influence the frequency of these indices in each QRS group.*

***Conclusion:*** *The prevalence of both inter and intraventricular dyssynchrony indices was greater in the patients with wide QRS than in those with narrow QRS duration. The underlying etiology may affect the frequency of interventricular but not intraventricular dyssynchrony indices.*

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## Introduction

Dyssynchrony is a frequent feature in severe heart failure (HF) patients.[1-3] It is well-established that short- and long-term cardiac resynchronization therapy (CRT) can improve cardiac function and enhance functional capacity in advanced chronic heart failure.[4-6] The prevalence of responders to CRT has been widely varied amongst patients. Presence of left ventricular (LV) dyssynchrony indices is the most powerful predictor of favorable response and long-term survival in both ischemic and non-ischemic HF after biventricular pacing[1, 7-12] and recent studies have deducted that the severity of systolic dyssynchrony is a much better predictor of such a response in comparison to QRS complex duration.[1] Thus, assessment of the severity of systolic dyssynchrony is the key to the appropriate selection of patients. Tissue Doppler imaging (TDI) has been widely used to assess segments' time-to-peak myocardial sustained systolic velocity (Ts) and investigate parameters of systolic dyssynchrony in patients receiving CRT.[7, 8, 12-15]

Etiology of HF and QRS duration are two parameters which may influence the LV dyssynchrony pattern and subsequently affect the favorable response.[12] Previous studies investigated LV dyssynchrony indices in HF patients according to QRS duration[2, 3, 10, 16] or underlying etiology;[2, 16] however, there are not enough comprehensive studies evaluating various dyssynchrony indices with respect to both of these confounders. The current study aimed to evaluate potential differences in the prevalence of inter and intraventricular dyssynchrony indices in terms of the cause of HF in patients with various QRS durations. The result would be helpful for the future investigators to have a more accurate prevision on electro conduction differences in HF patients and better control the possible confounders which could influence their studies.

## Methods

From August 2005 to November 2010, we retrospectively reviewed the available data on echocardiographic imaging of 230 refractory HF patients (age = 52.9 ± 16.6 years, 73.5% male) with refractory HF who were referred to our department for echocardiographic evaluation. All the patients were still symptomatic (New York Heart Association [NYHA] functional class III or IV) despite optimized drug treatment as defined by the current guideline[17] and had left ventricular ejection-fraction (LVEF) of ≤ 35%. Patients with previous pacemaker implantation and those with right bundle branch block (RBBB) were excluded from the study. All the patients underwent complete resting conventional echocardiography and TDI for the evaluation of the extent of LV dyssynchrony. The patients were divided into three categories according to the QRS duration: 57 patients with QRS duration < 120 ms; 76 with QRS duration 120 – 150 ms; and 97 patients with QRS duration ≥ 150 ms. The underlying cause was ischemic cardiomyopathy (ICM) in 99 patients and dilated cardiomyopathy (DCM) in 131 patients. The etiology was diagnosed as ischemia if the patients had angiographic evidence of significant coronary artery disease (at least narrowing ≥ 70% in one epicardial coronary artery) with corresponding wall motion abnormality; otherwise, they were categorized as DCM. Medication included loop diuretics in 44.8%, beta blockers in 85.9%, Spirinolacton in 66%, angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blockers in 87.2%, Digoxin in 54.6%, and ASA in 95%. The study protocol was approved by the institutional ethics committee review board of the hospital.

Standard twelve-lead electrograms were acquired at a paper speed of 25 mm/s and a scale of 10 mm/mV. The measurements of the QRS duration (recorded from the surface leads, demonstrating the greatest values) and the assessment of the QRS axis and morphology were performed by an experienced observer, and complete or incomplete left bundle branch block (LBBB) was diagnosed in twelve-lead surface electrocardiography (ECG) using the guideline definition.[18]

Complete two-dimensional transthoracic echocardiography, M-mode, pulsed, and continuous-wave Doppler with color-flow imaging was performed using a commercially available ultrasonographic system (VIVID 7, Vingmed GE, Horten, Norway with a 3.5-MHz transducer). All the following parameters were measured in keeping with the guidelines of the American Society of Echocardiography:[19] right and left ventricular dimensions (VD), pulmonary artery pressure (PAP), and tricuspid annular plane systolic excursion (TAPES). Additionally, left ventricular end systolic and diastolic volume and LVEF were measured by the multi-plane modality of a four-dimensional probe employing the Simpson technique. According to the currently used grading system, the severity of mitral regurgitation was scored 1 as mild, 2 as moderate, 3 as moderate to severe, and 4 as severe and tricuspid regurgitation was graded 1 as mild, 2 as moderate, and 3 as severe regurgitation.[20]

Interventricular dyssynchrony was assessed by measuring the opening and closing times of the aortic and pulmonic valves using the systolic blood flow by pulsed Doppler with the sample volume placed at the level of the aortic and pulmonic annulus. The aortic pre-ejection time was measured from the beginning of the QRS complex to the beginning of the aortic flow velocity curve recorded by pulsed-wave Doppler in the apical view. Similarly, the pulmonary pre-ejection time was measured from the beginning of the QRS complex to the beginning of the pulmonary flow velocity curve recorded in the left parasternal short-access view. The difference between the two values determined the interventricular mechanical delay (IVMD). A cut-off value of 40 ms was considered for interventricular dyssynchrony.[21]

Systolic synchronicity was assessed via TDI using the apical views (four-chamber, two-chamber, and long-axis) of the LV as previously described[22] with adjustments of filter frequency, gain settings, pulse repetition frequency, and color saturation. At least three consecutive beats were stored, and the images were digitally stored for off-line analysis. The following twelve segments were interrogated: septal, lateral, anterior, inferior, antroseptal, and posterior at both basal and middle levels. The timing of the systolic events was evaluated by measuring Ts in each LV segment with reference to the onset of the QRS complex. The following seven indices of systolic dyssynchrony were computed, and the predictive cut-off values for positive response to CRT are shown in parentheses in line with the previously reported data:

- All segments delay (Ts-all-delay): Differences between the longest and shortest Ts in twelve LV segments (105 ms).[23]
- Basal segments delay (Ts-basal-delay): Differences between the longest and shortest Ts in six LV basal segments (78 ms).[23]
- All segments standard deviation (Ts-all-SD): Standard deviation (SD) of Ts from all twelve LV segments (34.4 ms).[23]
- Basal segments standard deviation (Ts-basal-SD): SD of Ts from six LV basal segments (34.5 ms).[23]
- Septal to lateral delay (Sep-lat-delay): Absolute difference in Ts between the basal interventricular septum and the lateral wall (65 ms).[24, 25]
- Anteroseptal-posterior delay (Antsep-pos-delay): Absolute difference in Ts between the basal-posterior and anteroseptal segments (65 ms).[24]
- Anterior-inferior delay (Ant-inf-delay): Absolute difference in Ts between the basal anterior and inferior segments (65 ms).[24]

According to our previous published data, the intraobserver and interobserver variability for TDI measurements for time-to-peak systolic velocity was 13 ± 11% and 18 ± 20%, respectively.[22]

The results are reported as mean ± standard deviation (SD) for the quantitative variables and are summarized by absolute frequencies and percentages for the categorical variables. The continuous variables were compared using one-way analysis of variance (ANOVA) or Kruskal-Wallis test when the presumption of normality was not met or in case of unequal variances, while the categorical variables were compared using the chi-square test or Fisher exact test when more than 20% of the cells with an expected count of $< 5$ were observed. Between the two subgroups of the ICM and DCM patients, the continuous variables were compared using the independent two-sample t-test or the nonparametric Mann-Whitney U test whenever the data did not appear to have normal distributions, and the categorical variables were compared using the chi-square or Fisher exact test, as appropriate.

The influence of QRS duration (classified as $< 120$ ms, 120 -150 ms, and $\geq 150$ ms) on the conventional echocardiographic measurements and cardiac dyssynchrony indices was appraised by constructing multiple linear regression (for continuous indices), logistic regression (for binary indices), or proportional odds model (the most commonly used model among the types of cumulative logit models for ordinal responses[26]) for the ordinal indices, including mitral valve regurgitation (MR) and tricuspid valve regurgitation (TR) grades, while accounting for the confounding effects of age, sex, underlying etiology, and presence or absence of left bundle branch block (LBBB). Additionally, the above multivariable analyses were conducted separately in each subgroup of QRS ($< 120$ ms, 120 -150 ms, and $\geq 150$ ms) to assess the possible effect of the underlying etiology on the cardiac dyssynchrony indices, while controlling for age, sex, and QRS duration.

For the statistical analysis, the statistical software SPSS version 13.0 for Windows (SPSS Inc., Chicago, IL) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA) were used. All the p values were considered two-tailed, with statistical significance defined by p value $\leq 0.05$.

## *Results*

The patients' demographic data, clinical characteristics, and conventional echocardiographic measurements are presented in Table1. There was a significant difference in age between the patient groups according to the QRS duration and also cardiomyopathy etiology. The subjects with QRS duration $\geq 150$ ms and those with ICM were significantly older then the corresponding groups, and male sex was significantly more frequent amongst the ICM rather than the DCM patients. In regard to the cardiac conduction pattern, the occurrence of LBBB appeared to be significantly raised in the subjects with prolonged QRS duration. For the standard echocardiographic parameters, no significant difference was found between the patients in terms of the QRS duration or underlying etiology except for tricuspid regurgitation severity, which was greater in the patients with QRS duration $< 120$ ms than in both groups of patients with QRS duration 120-150 and QRS duration $\geq 150$ ms. There was no significant difference between the patients groups in terms of medication.

According to the substantial differences in the demographic, underlying etiology, and prevalence of LBBB between the groups, all the subsequent comparisons were adjusted for these variables as appropriate.

Table 2. Shows that aortic pre-ejection time associated with both QRS duration and underlying etiology. The patients with wide QRS duration or DCM revealed a longer aortic pre-ejection time and higher proportion of interventricular

dyssynchrony than the corresponding groups. In regard to the pulmonary pre-ejection period, no significant difference was found between the groups according to the QRS duration or underlying etiology.

Figure1 shows that, irrespective of the etiology, Ts in patients with QRS duration ≥ 150 ms was much more delayed in all the twelve LV segments than the corresponding segments in those with QRS duration < 120 ms. Figure 2 indicates that overall the underlying etiology did not influence Ts in the individual LV segments in the QRS groups.

Amongst the intraventricular dyssynchrony indices, Dys-Ts-all and Dys-Ts-bas indices were significantly much more frequent in the patients with wide QRS duration than in those with a narrow QRS duration. In regard to the dyssynchrony indices derived from SD of Ts, neither Dys-Ts-all-SD nor Dys-Ts-bas-SD revealed a significant difference between the

Table1. Demographic data, clinical characteristics and conventional echocardiographic measurement in patients according to QRS duration and cause of heart failure

| | Total patients (n=230) | QRS duration | | | | | | | | | P value# |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | <120 ms | | | 120-150 ms | | | ≥150 ms | | | |
| | | Total (n=57) | ICM (n=25) | DCM (n=32) | Total (n=76) | ICM (n=33) | DCM (n=43) | Total (n=97) | ICM (n=41) | DCM (n=56) | |
| Age (y) | 52.9±16.6 | 45.6±12.5 | 54.7±10.4 | 40.6±16.0$^{+}$ | 51.7±16.4 | 60.8±11.0 | 47.5±15.5$^{+++}$ | 56.1±19.3$^{**}$ | 61.4±13.4 | 52.7±18.8$^{++}$ | 0.002 |
| Male gender | 169(73.5) | 43(75.4) | 22(88.0) | 21(65.6)$^{+}$ | 59(77.6) | 32(97.0) | 27(62.8)$^{+++}$ | 67(69.1) | 32(78.0) | 35(62.5) | 0.417 |
| LBBB | 80(34.8) | 8(14.0) | 3(12.0) | 5(15.6) | 16(21.1) | 6(18.2) | 10(23.3) | 56(57.7)$^{***\dagger\dagger}$ | 23(56.1) | 33(58.9) | <0.001 |
| DM | 33(29.7) | 7(35.0) | 5(50.0) | 2(20.0) | 8(23.5) | 4(33.3) | 4(18.2) | 18(31.6) | 9(36.0) | 9(28.1) | 0.611 |
| AF | 9(3.9) | 1(1.8) | 0 | 1(3.1) | 4(5.3) | 1(3.0) | 3(7.0) | 4(4.1) | 0 | 4(7.1) | 0.132 |
| NYHA Class | | | | | | | | | | | 0.598 |
| II | 16(16.2) | 1(4.8) | 1(10.0) | 0 | 6(21.4) | 4(44.4) | 2(10.5) | 9(18.0) | 4(21.1) | 5(16.1) | |
| III | 65(65.7) | 16(76.2) | 7(70.0) | 9(81.8) | 17(60.7) | 4(44.4) | 13(68.4) | 32(64.0) | 12(63.2) | 20(64.5) | |
| IV | 18(18.2) | 4(19.0) | 2(20.0) | 2(18.2) | 5(17.9) | 1(11.1) | 4(21.1) | 9(18.0) | 3(15.8) | 6(19.4) | |
| LVEF (%) | 21.6±7.0 | 20.6±5.5 | 22.7±6.8 | 19.4±6.9 | 20.9±6.6 | 22.4±5.9 | 20.8±7.2 | 21.2±6.2 | 22.0±7.1 | 22.3±7.3 | 0.856 |
| PAP (mmHg) | 41.6±15.2 | 50.3±18.4 | 49.2±20.1 | 44.2±14.1 | 41.0±17.4 | 36.9±17.0 | 41.7±15.3 | 40.2±13.7 | 40.7±12.8 | 39.4±13.0 | 0.074 |
| LVDs (mm) | 56.7±13.1 | 58.3±8.0 | 55.4±8.5 | 59.1±9.8 | 61.7±23.2 | 61.3±23.4 | 57.6±12.6 | 55.2±9.7 | 54.8±9.2 | 53.8±10.1 | 0.257 |
| LVDd (mm) | 65.0±9.9 | 67.1±7.4 | 64.0±9.2 | 66.4±9.0 | 66.4±12.1 | 66.9±8.8 | 64.9±11.6 | 66.9±8.8 | 63.8±9.5 | 64.4±10.7 | 0.739 |
| LVEDV($mm^3$) | 175.4±71.7 | 190.1±70.8 | 185.4±71.8 | 176.3±65.1 | 188.1±95.1 | 182.6±48.3 | 180.2±98.1 | 166.5±64.3 | 173.2±56.4 | 165.6±74.7 | 0.667 |
| LVESV ($mm^3$) | 136.5±68.7 | 151.9±65.7 | 144.3±68.8 | 144.5±60.8 | 146.3±91.1 | 141.6±47.8 | 140.9±92.7 | 125.7±62.6 | 131.5±48.1 | 127.0±74.7 | 0.582 |
| MR grade | 1.7±0.9 | 2.0±0.7 | 1.7±0.6 | 1.9±0.9 | 1.7±0.9 | 1.6±0.8 | 1.6±1.0 | 1.6±0.9 | 1.7±0.9 | 1.6±0.8 | 0.467 |
| TR grade | 1.2±0.8 | 1.7±0.8 | 1.6±0.9 | 1.7±0.9 | 1.0±0.9$^{*}$ | 1.0±0.7 | 1.2±0.9 | 1.0±0.8$^{*}$ | 1.2±0.7 | 1.0±0.8 | 0.045$^{\Phi}$ |
| RVD (mm) | 32.7±8.2 | 36.7±9.7 | 35.6±7.9 | 36.4±9.8 | 33.5±7.3 | 29.8±7.1 | 34.6±7.3 | 30.8±8.5 | 31.3±7.5 | 30.5±8.4 | 0.087 |
| TAPES (mm) | 15.7±4.9 | 15.3±7.3 | 14.2±7.4 | 15.1±5.5 | 15.6±4.3 | 16.3±3.7 | 15.6±4.8 | 16.1±4.3 | 15.3±3.8 | 16.7±4.6 | 0.512 |

Data are presented as mean±SD or n (%)

ICM, Ischemic cardiomyopathy; DCM, Dilated cardiomyopathy; LBBB, Left bundle branch block; DM, Diabetes mellitus; AF, Atrial fibrillation; NYHA, New York Heart Association; LVEF, Left ventricle ejection fraction; PAP, Pulmonary artery pressure; LVDs, Systolic left ventricle dimension; LVDd, Diastolic left ventricle dimension; LVEDV, Left ventricle end diastolic volume; LVESV, Left ventricle end systolic volume; MR, Mitral regurgitation; TR, Tricuspid regurgitation; RVD, Right ventricle dimension; TAPES, Tricuspid annular plane systolic excursion

#Overall P value in comparison of QRS groups

*P value < 0.05 **P value < 0.01 ***P value < 0.001 in comparison with group of QRS < 120 ms

†P value < 0.05

††P value < 0.001 in comparison with group of 120 ms < QRS < 150 ms

+P value < 0.05 ++P value < 0.01 in compression of DCM vs. ICM ΦP value is adjusted for age, sex, etiology and LBBB

Table 2. Echocardiographic indices of inter and intraventricular dyssynchrony according to QRS duration and underlying etiology

| | Total patients (n=230) | QRS duration | | | | | | | | | P value# |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | <120 ms | | | 120-150 ms | | | ≥150 ms | | | |
| | | Total (n=57) | ICM (n=25) | DCM (n=32) | Total (n=76) | ICM (n=33) | DCM (n=43) | Total (n=97) | ICM (n=41) | DCM (n=56) | |
| QRS duration | 145.4±33.9 | 104.7±11.2 | 105.8±11.0 | 103.8±11.5 | 134.6±8.1$^{***}$ | 135.5±8.2 | 134.0±8.0 | 177.9±22.0$^{***\dagger\dagger\dagger}$ | 185.3±24.4 | 172.4±18.4$^{++}$ | 0.000 |
| Aorta Pre-ejection period (ms) | 128.1±37.1 | 112.8±19.2 | 95.9±19.7 | 115.5±19.6+ | 135.3±57.3$^{**}$ | 114.5±21.3 | 132.8±54.1+ | 139.9±33.2$^{***\dagger}$ | 137.3±33.0 | 147.5±30.1$^{+}$ | <0.001 |
| Pulmonary Pre-ejection period (ms) | 92.6±28.6 | 90.3±18.3 | 80.9±16.3 | 90.7±15.6 | 103.9±53.2 | 90.1±20.7 | 103.4±49.7 | 92.4±23.1 | 94.7±22.9 | 90.4±21.7 | 0.061 |
| IVMD (ms) | 37.6±26.1 | 23.8±15.6 | 19.8±13.6 | 27.9±17.7 | 31.6±20.1 | 26.1±20.5 | 30.3±18.5 | 48.1±26.4$^{***\dagger\dagger\dagger}$ | 45.9±26.6 | 57.5±27.8$^{+}$ | <0.001 |
| Interventricular dys (cut-off: 40 ms) | 96(41.7) | 11(19.3) | 3(12.0) | 8(25.0) | 22(28.9)$^{*}$ | 7(21.2) | 15(34.9)+ | 63(64.9)$^{***\dagger\dagger\dagger}$ | 20(48.8) | 43(76.8)$^{++}$ | <0.001 |
| Ts-all-delay (ms) | 113.3±44.9 | 102.3±36.3 | 89.4±35.9 | 105.6±33.5 | 117.0±42.3$^{**}$ | 118.1±54.3 | 120.8±48.0 | 116.6±40.3$^{*}$ | 114.0±48.9 | 119.9±40.5 | 0.031 |
| Dys Ts-all (cut-off: 105 ms) | 122(55.5) | 22(39.3) | 8(32.0) | 14(45.2) | 43(60.6)$^{*}$ | 18(56.3) | 25(64.1) | 57(61.3)$^{*}$ | 24(60.0) | 33(62.3) | 0.030 |
| Ts-all-SD (ms) | 40.1±16.7 | 37.3±14.5 | 32.0±13.4 | 38.4±12.7 | 41.5±14.4 | 41.2±23.7 | 41.4±15.4 | 41.3±15.0 | 41.2±17.2 | 42.1±15.0 | 0.089 |
| Dys Ts-all-SD (cut-off:34.4 ms) | 76 (40.2) | 22(46.8) | 8(36.4) | 14(56.0) | 40(60.6) | 15(53.6) | 25(65.8) | 51(67.1) | 18(66.7) | 33(67.3) | 0.169 |
| Ts-6-delay (ms) | 97.3±43.4 | 88.1±38.7 | 77.8±35.4 | 89.7±36.8 | 97.6±39.7 | 96.7±49.8 | 101.5±45.4 | 101.5±36.3 | 105.2±52.4 | 102.1±36.0 | 0.078 |
| Dys Ts-6 (cut-off: 78 ms) | 143(65.6) | 29(51.8) | 11(40.0) | 18(58.1) | 48(69.6)* | 18(60.6) | 28(71.8) | 68(73.1)$^{**}$ | 26(65.0) | 42(79.2) | 0.025 |
| Ts-6-SD (ms) | 40.0±18.6 | 35.5±15.8 | 31.4±14.3 | 37.1±14.6 | 41.1±18.1 | 42.7±27.2 | 40.0±17.2 | 41.7±15.9 | 43.5±21.0 | 41.3±15.4 | 0.086 |
| Dys Ts-6-SD (cut-off: 34.5 ms) | 125(54.3) | 23(40.4) | 9(36.0) | 14(43.8) | 42(55.3) | 17(51.5) | 25(58.1) | 60(61.9) | 26(63.4) | 34(60.7) | 0.066 |
| Sep-lat- delay (ms) | 55.8±37.7 | 56.9±35.9 | 42.8±31.8 | 59.1±36.8 | 58.9±33.9 | 46.9±27.9 | 61.2±32.7 | 58.1±39.3 | 61.0±52.6 | 57.1±35.5 | 0.832 |
| Dys sep-lat (cut-off: 6 ms) | 72(31.3) | 18(31.6) | 7(28.0) | 11(34.4) | 28(36.8) | 7(21.2) | 21(48.8) | 26(26.8) | 9(22.0) | 17(30.4) | 0.237 |
| Antsep-post-delay (ms) | 56.3±41.9 | 45.8±45.4 | 37.8±32.5 | 49.5±42.8 | 54.3±47.6 | 68.8±53.0 | 55.3±37.5 | 59.6±40.9 | 65.4±42.0 | 57.4±37.4 | 0.143 |
| Dys Antsep-post (cut-off: 65 ms) | 83(36.2) | 14(24.6) | 5(20.0) | 9(28.1) | 29(38.6) | 14(42.4) | 15(35.7) | 40(41.2) | 19(46.3) | 21 (37.5) | 0.308 |
| Ant-inf-delay (mm) | 56.9± 40.9 | 50.8±23.5 | 47.6±33.3 | 50.6±28.0 | 59.5±38.0 | 56.7±58.0 | 58.8±35.7 | 64.8±41.4 | 56.4±39.2 | 63.5±43.2 | 0.232 |
| Dys Ant-inf (cut-off: 65 ms) | 82(35.7) | 17(29.8) | 7(28.0) | 10(31.3) | 25(32.9) | 8(24.2) | 17(39.5) | 40(41.2) | 14(34.1) | 26(46.4) | 0.302 |

Data are presented as mean±SD or n (%)

IVMD, Interventricular mechanical delay; Ts-all, All segments delay; Dys, Dyssynchrony; SD, Standard deviation; Ts-all-SD, All segments SD; Ts-6, Basal segments delay; Ts-6-SD, Basal segments; SD, Sep-lat-delay Septal-lateral delay; Antsep-pos-delay, Antroseptal-posterior delay; Ant-inf-delay: Anterior inferior delay

#Overall P value in comparison of QRS groups adjusted for age; sex, etiology and left bundle branch block

*P value < 0.05 **P value < 0.01 ***P-value < 0.001 in comparison with group of QRS < 120 ms

†P value < 0.05 ††P value < 0.01

†††P value < 0.001 in comparison with group of 120 ms < QRS < 150 ms. All compression between ICM and DCM groups are adjusted for age, sex and QRS duration +P value < 0.05 ++P value < 0.01 in compression of ICM vs. ICM

QRS groups. Etiology did not appear to influence any of the intraventricular dyssynchrony indices.

With respect to the opposite wall dyssynchrony indices, there was no difference in the frequency of dyssynchrony between the QRS groups or between the patients with ICM and DCM in the matched QRS groups.

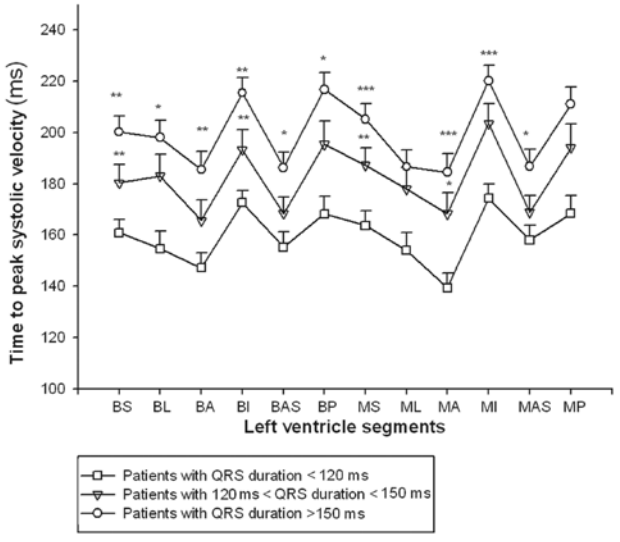


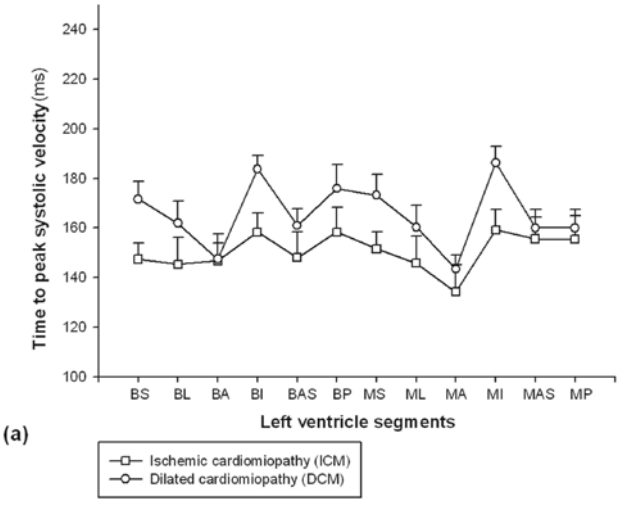

Figure1. Comparison of the time-to-peak systolic myocardial velocities (Ts) in individual left ventricular segments in heart failure patients according to the QRS duration subgroups: All the compressions between the QRS groups are adjusted for age, sex, etiology, and LBBB

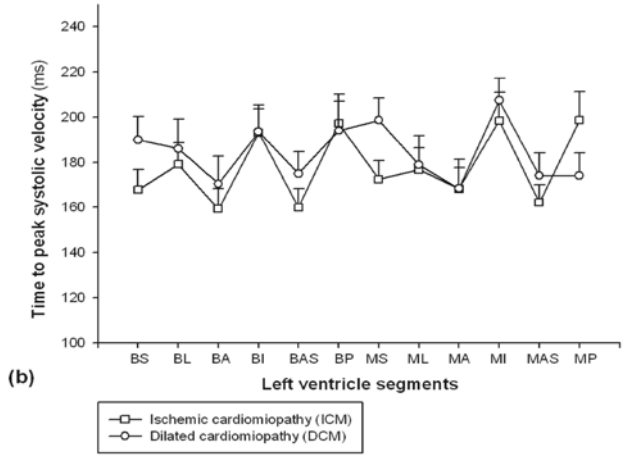
BS, Basal-septal; BL, Basal-lateral; BA, Basal-anterior; BI, Basal-inferior; BAS, Basal-anteroseptal; BP, Basal-posterior; MS, Mid-septal; ML, Mid-lateral; MA, Mid-anterior; MI, Mid-basal inferior; MAS, Mid-basal anteroseptal; MP, Mid-basal posterior)

*p value < 0.05

**p value < 0.01

***p value < 0.001 in comparison with the group of QRS < 120 ms



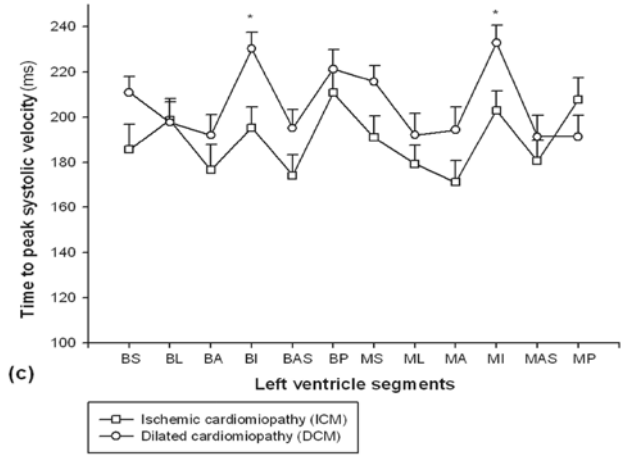




Figure 2. Comparison of the time-to-peak systolic myocardial velocities (Ts) in individual left ventricular segments according to the underlying etiology in patients with QRS duration (a) < 120 ms (b) 120 – 150 ms (C) ≥ 150 ms. All the compressions between the Ischemic cardiomyopathy (ICM) and Dilated cardiomyopathy (DCM) groups are adjusted for age, sex, and QRS duration

*P value < 0.05 in the comparison of DCM&ICM

BS, Basal-septal; BL, Basal-lateral; BA, Basal-anterior; BI, Basal-inferior; BAS, Basal-anteroseptal; BP, Basal-posterior; MS, Mid-septal; ML, Mid-lateral; MA, Mid-anterior; MI, Mid-basal inferior; MAS, Mid-basal anteroseptal; MP, Mid-basal posterior

## *Discussion*

The present study illustrates that the prevalence of interventricular dyssynchrony was significantly higher in patients with a wide QRS duration (≥ 120 ms) than in those with a narrow QRS duration (< 120 ms). Likewise, etiology appeared to influence interventricular dyssynchrony since it was more prevalent in the patients with DCM than in

those with ICM in each of QRS groups. Turning to the TDI measurements, the Ts of the individual LV segments were much more prolonged in the patients with QRS ≥ 150 ms than the corresponding segments in those with QRS < 120 ms. The Dys-Ts-all and Dys-Ts-bas indices were significantly much more frequent in the patients with a wide QRS duration than in those with a narrow QRS duration, and a similar, albeit not significant, trend was found as regards the SD dyssynchrony indices between the QRS groups. Etiology did not appear to affect either Ts or the intraventricular dyssynchrony indices. In terms of the opposite wall dyssynchrony indices such as Dys-sept-lat, Dys-ant-infer, and Dys-antrsep-post, no significant difference was found with respect to the prevalence of these indices according to the QRS groups or underlying etiology.

Chiming in with our results, Ghio et al. and Bleeker et al. also reported significant age but not gender differences between their patient groups with respect to QRS duration: HF patients with a QRS duration ≥ 150 ms were significantly older than were those with a narrow QRS duration < 120 ms.[2, 27] In regard to the underlying etiology in our study, the patients with ICM were significantly older than those with DCM, and ICM was a much more dominant feature in the males than in the females in all the QRS groups. These results were not unexpected since male gender and age both are well-recognized risk factors for ischemic heart disease. Van de veire et al. also reported a similar pattern in age difference between ICM and DCM patients.[28]

We found that TR severity was significantly greater in the patients with QRS duration < 120 ms than in those with QRS duration 120-150 or ≥ 150 ms. This result cannot be explained easily. Although we neutralized the potential confounding effect of age, sex, etiology, and difference in the frequency of LBBB by including these variables into our multivariate analysis, it seems that other potential confounders such as the presence/absence of pulmonary hypertension or heart rate might have influenced the results.

### *Interventricular dyssynchrony indices*

Based on our results, the prevalence of interventricular dyssynchrony increased from 19.3% in the patients with QRS < 120 ms to 64.9% in those with QRS ≥ 150 ms duration. These findings are consistent with previous studies demonstrating a higher prevalence of interventricular dyssynchrony in patients with a wide QRS duration than in those with a narrow QRS duration.[2, 3, 29, 30] Likewise, the frequency of interventricular dyssynchrony in those with QRS duration 120-150 and ≥ 150 ms was significantly higher in the DCM than in the ICM patients, while a similar trend was also seen in those with QRS duration < 120 ms. By contrast, Ghio et al. and Haghjoo et al. did not find any significant relationship between etiology and IVMD.[2, 30] This inconsistency may be due to disregarding the confounding effect of the QRS duration in the comparison of the IVMD between the DCM and ICM groups by previous investigators. Nevertheless, in the current study, all the comparisons were conducted regarding the potential confounding effect of the demographic and QRS duration differences between the groups. Furthermore, a larger recruited sample size seems to have slightly raised the power of our study.

Regional Ts in all the segments were consistently prolonged in the patients with QRS duration ≥ 150 ms compared with the corresponding segments in those with QRS duration < 120 ms. Accordingly, Ghio et al. reported a similar delay in the comparison of segmental Ts between patients with wide and narrow QRS durations.[2] In regard to the underlying etiology, there was no significant difference in the segmental Ts between the DCM or ICM patients in the matched QRS groups except for Ts in the inferior region in the patients with QRS ≥ 150 ms, which was significantly more delayed than the corresponding region in the ICM patients. Contrary to our findings, Van de Veire reported more prolonged Ts in nearly all the LV segments in patients with DCM than in those with ICM in the presence of QRS duration ≤ 120 ms.[28] To explain the difference it is deserving of note that all the Ts in the Van de Veire study were corrected for the heart rate, whereas we did not apply any such correction in the current study.

According to the intraventricular dyssynchrony indices, Dys-Ts-all and Dys-Ts-basal were more prevalent in the patients with QRS duration ≥ 150 ms and 120-150 ms than in those with QRS duration < 120 ms. These data are consistent with those in previous studies indicating a higher frequency of Dys-Ts-all[1, 30] Dys-Ts-basal[28] indices in patients with a wide QRS than in those with a narrow QRS. Other studies have also reported similar interventricular dyssynchrony prevalence in different QRS groups using various definitions for intraventricular dyssynchrony indices.[2, 3, 31] Neither SD-Ts nor the opposite wall dyssynchrony indices revealed similar differences in the comparison of the QRS groups. In contrast, Yu et al. reported significant differences in the frequency of SD-Ts dyssynchrony index between patients with wide and narrow QRS.[1] Van de Veire also reported similar results in the echocardiographic evaluation of DCM patients.[28] It should be noted that in these studies, dyssynchrony was defined using a cut-off point different from what we applied in our study. Bleeker et al., in a study of 90 HF patients, reported a greater septum-to-lateral wall delay in patients with a wide QRS duration than in those with a narrow QRS duration; they, however, did not find any significant regressive relationship between QRS duration and septal-to-lateral delay.[27] Etiology did not appear to influence any of the intraventricular dyssynchrony indices in the matched QRS duration groups. Likewise, previous studies have not indicated any difference in intraventricular dyssynchrony indices between DCM and ICM patients.[2, 28]

The segmental Ts values were not corrected for the heart

rate in the current study. The use of this type of adjustment may lead to more accurate and concise results in future studies.

## Conclusion

The prevalence of both interventricular dyssynchrony indices and two of the main intraventricular dyssynchrony indices (Dys-Ts-all and Dys-Ts-basal) was greater in the patients with a wide QRS duration than in those with a narrow QRS duration. The underlying etiology may have influenced the frequency of the interventricular but not intraventricular dyssynchrony indices: patients with DCM demonstrated a higher level of interventricular dyssynchrony than did those with ICM. Neither the QRS groups nor the etiology affected the opposite wall dyssynchrony indices. The findings would help future studies investigating the predictive role of dyssynchrony indices on the CRT outcome to better adjust the confounders (such as QRS duration and underlying etiology) in comparisons between groups.

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