# Prevalence of Mechanical Dyssynchrony in Heart Failure Patients with Different QRS Durations

MAJID HAGHJOO, M.D.,* ATAALLAH BAGHERZADEH, M.D.,*
AMIR FARJAM FAZELIFAR, M.D.,* ZAHRA OJAGHI HAGHIGHI, M.D.,†
MARYAM ESMAIELZADEH, M.D.,† ABOLFATH ALIZADEH, M.D.,*
ZAHRA EMKANJOO, M.D.,* ANITA SADEGHPOUR, M.D.,† NILOOFAR SAMIEI, M.D.,†
MARYAM MOSHKANI FARAHANI, M.D.,† MOHAMMAD ALI SADR-AMELI, M.D.,*
MAJID MALEKI, M.D.,† and FEREIDOUN NOOHI, M.D., F.A.C.C.†

From the *Department of Pacemaker and Electrophysiology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Mellat Park, Tehran, Iran, and the †Department of Echocardiography, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Mellat Park, Tehran, Iran

***Background:*** *Cardiac resynchronization therapy (CRT) has emerged as an established therapy for congestive heart failure. However, up to 30% of patients fail to respond to CRT despite prolonged QRS.*

***Objectives:*** *This study aimed at defining the prevalence of interventricular and intraventricular dyssynchrony in heart failure patients with different QRS durations.*

***Methods:*** *A total of 123 consecutive patients with severe heart failure (LVEF < 35% and NYHA class III–IV) were prospectively evaluated using 12-lead electrocardiogram and complete echocardiographic examination including tissue Doppler imaging.*

***Results:*** *According to the QRS duration, 56 patients had a QRS duration ≤120 ms (Group 1), 33 patients had a QRS duration between 120 and 150 ms (Group 2), and 34 patients had a QRS duration ≥150 ms (Group 3). Intraventricular dyssynchrony was present in 36% of Group 1 patients, in 58% of Group 2 patients, and in 79% of Group 3 patients (P < 0.000). Linear regression demonstrated a weak relation between QRS and intraventricular dyssynchrony. A greater proportion of patients with interventricular dyssynchrony was observed in Group 3 or Group 2 compared to patients with normal QRS duration (32% in Group 1 vs. 51.5% in Group 2 vs. 76.5% in Group 3, P < 0.000). Linear regression demonstrated a significant relation between QRS duration and interventricular mechanical delay.*

***Conclusions:*** *Although both interventricular and intraventricular dyssynchrony increased with the increasing QRS duration, the correlation between intraventricular mechanical and electrical dyssynchrony was weak. The lack of intraventricular dyssynchrony in a fraction of patients with standard CRT indication by QRS duration may provide us insight into the nonresponders rates. (PACE 2007; 30:616–622)*

***congestive heart failure, electrocardiography, interventricular delay, intraventricular delay, Tissue Doppler echocardiography***

## Introduction

Cardiac resynchronization therapy (CRT) has emerged as an established therapy for congestive heart failure (CHF) due to severe left ventricular (LV) systolic dysfunction.[1–4]

Recent large-scale clinical trials have confirmed the favorable effects of CRT on symptoms, quality of life, exercise capacity, left ventricular function, and also showed that CRT significantly reduces mortality risk.[5,6] Current selection criteria for patients eligible for CRT include: end-stage CHF with New York Heart Association (NYHA) class III–IV, depressed left ventricular ejection fraction (LVEF) <35%, and QRS duration >130 ms.[1,2,7–10] Despite these criteria, approximately 30% of the patients fail to respond to CRT despite prolonged QRS duration.[10–16] More recently, it has been pointed out that even patients with normal QRS duration may exhibit dyssynchrony and also potentially treatable by CRT.[12,15,16] There are other observations that have raised the concerns over the real value of the QRS duration in predicting mechanical dyssynchrony: during single-chamber left ventricular pacing alone, the QRS duration is usually longer than during intrinsic QRS with left bundle branch block (LBBB) morphology, which contrasted with a significant increase

Address for reprints: Majid Haghjoo, M.D., Department of Pacemaker and Electrophysiology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Mellat Park, Vali-E-Asr Avenue, Tehran 1996911151 Iran, P.O. Box: 15745–1341. Fax: 0098-21-2204-8174. e-mail: majid.haghjoo@gmail.com

There is no conflict of interest or financial support for any of authors who participated in this study.

Received November 20, 2006; revised January 9, 2007; accepted January 29, 2007.

of LV contractility and improvement of stroke volume.[17] Together these findings question the extent to which QRS duration is linked to mechanical dyssynchrony.

Therefore, we designed this study aimed at defining the prevalence of interventricular and intraventricular dyssynchrony in heart failure patients with different QRS durations.

## Methods

### Characteristics of CHF Population

Between January 2004 and October 2005, a total of 123 consecutive patients with severe heart failure were prospectively included. Inclusion criteria were CHF with NYHA class III–IV and advanced LV systolic dysfunction (LVEF < 35%). We excluded patients with nonsinus rhythm, previous pacemaker implantation, and valvular heart disease. The study was approved by the local Ethics Committee, and written informed consent was obtained from all the patients. Included were 91 men and 32 women with mean age 55 ± 15 years. The underlying etiology was ischemic heart disease in 62% of patients and primary dilated cardiomyopathy in remaining 38% of patients. According to the QRS duration, the patients were classified into three groups: Group 1, 56 patients with a narrow QRS duration (≤120 ms); Group 2, 33 patients with intermediate QRS duration (between 120 and 150 ms); Group 3, 34 patients with wide QRS duration (≥150 ms). All patients were in NYHA class III (n = 103) or IV (n = 20). All patients underwent a standard 12-lead electrocardiography and a complete echocardiographic examination, including specific evaluation for inter- and intraventricular dyssynchrony.

### Electrocardiographic Analysis

Standard 12-lead electrocardiograms were acquired at a paper speed of 25 mm/s and a scale of 10 mm/mV. The measurements of QRS duration (recorded from the surface leads demonstrating the greatest values) and the assessment of QRS morphology were performed by two independent electrophysiologists who were blinded to the clinical status of the patients.

### Echocardiographic Protocol

A complete M-mode, two-dimensional and Doppler evaluation as performed using ultrasonographic equipment (Vivid 7, General Electric, Wauwatosa, WI, USA). Images were obtained using a 3.5-MHz transducer, at a depth of 16 cm in the parasternal and apical views (standard long-axis and two- and four-chamber views). LV end-systolic and diastolic dimensions and volumes and LV ejection fraction were calculated using the biplane Simpson's technique. Mitral regurgitation was graded according to the jet area method.

Pulse-wave Doppler recordings across the aortic and pulmonary valves were obtained from the apical 5-chamber view and parasternal short-axis view. The aortic pre-ejection time was calculated from the beginning of QRS complex to the beginning of the aortic flow velocity recorded in apical five-chamber view. The pulmonary pre-ejection time was measured from the beginning of QRS complex to the beginning of pulmonary flow velocity curve recorded in the left parasternal view. The difference between the two values was considered as the interventricular mechanical delay (IVMD); according to previous studies, an IVMD > 40 ms was selected as the cut-off value for interventricular dyssynchrony.[18,19]

Color tissue Doppler imaging (TDI) was acquired from the apical 4-chamber and 2-chamber views to assess myocardial regional function. In each view, both the basal and mid segments were assessed. In this way, the following segments were interrogated: septal, lateral, inferior, posterior, anteroseptal, and anterior at both the basal and middle levels. The regional pre-ejection period was measured for all segments from the beginning of QRS to the peak myocardial sustained systolic velocity ($T_S$). Maximal delta-$T_S$, defined as the maximal difference in $T_S$ among all 12 segments was used as the indicator of intraventricular dyssynchrony; a maximal delta-Ts > 100 ms was considered as the cut-off value for intraventricular dyssynchrony, based on previous studies.[16] All echocardiographic measurements were performed by two independent echocardiographers who were blinded to the clinical status of the patients.

### Statistical Analysis

Variables are expressed as mean ± SD for the continuous variables and as absolute or relative frequencies for categorical variables. $\chi^2$ analysis was used for categorical data and Fisher exact test for cell count less than five. Patient characteristics were compared by means of Student's *t*-test in case of continuous variables. Simultaneous comparison of more than two mean values was done by one-way analysis of variance (ANOVA) with Bonferroni correction. A general linear model was used to evaluate the association between different indicators of inter- and intraventricular dyssynchrony and QRS duration, while controlling for patients baseline characteristics. A two-tailed $P < 0.05$ was considered statistically significant. The software SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

## Results

### Characteristics of Study Population

By definition, all patients had severe heart failure; 103 were in NYHA class III and 20 in class IV. Etiology underlying the cardiomyopathy was ischemic in 62% and idiopathic in 38%. QRS duration and PR interval were 131.2 ± 30.5 ms (79–200 ms) and 191.4 ± 29.6 ms (110–280 ms), respectively. All patients were in sinus rhythm. Among the echocardiographic measurements, LV ejection fraction, LV end-systolic volume, and LV end-diastolic volume were 19 ± 6.5% (8–35%), 157.8 ± 61.4 mL, and 202 ± 68.6 mL, respectively.

The clinical characteristics of three QRS groups are summarized in Table I. The mean PR interval was longest in QRS Group 3 and shortest in QRS Group 1 (200 ± 26 vs. 181.6 ± 33 ms, P = 0.011). Among the three QRS groups, 76% of patients of Group 3, 60% of Group 2, and 41% of Group 1 had LBBB (P = 0.000).

Although there was a progressive increase in left ventricular volumes in parallel to QRS duration, this difference reached statistical significance only for LV end-systolic volume (P = 0.042). Increase in LV end-systolic and end-diastolic volumes resulted in comparable LV ejection fraction between the three QRS groups (Table II).

### Interventricular Dyssynchrony in Three QRS Groups

Although pulmonary pre-ejection period was similar in the three groups, there was a longer aortic pre-ejection period in Group 3 than in Group 1 and 2 patients (respectively, 137 vs. 117 vs. 113 ms, P = 0.03); this resulted in greater IVMD in Group 3 patients (respectively, 53 ± 21 ms vs. 42 ± 22 vs. 35 ± 21, P = 0.001). A greater proportion of patients with interventricular dyssynchrony was observed in the Group 3 or Group 2 compared to patients with normal QRS duration (32% in Group 1 vs. 51.5% in Group 2 vs. 76.5% in Group 3, P < 0.000). Linear regression demonstrated a significant relation between QRS duration and IVMD (n = 123, r = 0.56, P < 0.000) (Fig. 1). Etiology (idiopathic dilated vs. ischemic), gender, and QRS morphology had no relation to IVMD (all P > 0.05), whereas a higher proportion of patients with interventricular delay had NYHA class IV compared to patients without interventricular delay (26% vs. 11%, P = 0.03). Ejection fraction, LV end-diastolic volume, and LV end-systolic volume were similar in patients with and without interventricular delay (all P > 0.05).

### Intraventricular Dyssynchrony in Three QRS Groups

Intraventricular dyssynchrony (defined as maximal delta-Ts > 100 ms) was present in 36% of Group 1 patients, in 58% of Group 2 patients, and in 79% of Group 3 patients (P < 0.000). A stepwise increase in maximal delta-Ts was noted over the three groups, with mean maximal delta-Ts of 80 ms in Group 1, 92 ms in Group 2, and 110 ms in Group 3 patients (P < 0.000). Linear regression demonstrated significant relation between QRS duration and intraventricular dyssynchrony (n = 123, r = 0.35, P < 0.000), although a wide scattering of data

**Table I.**

Clinical Characteristics of Patients According to Three QRS Groups

| Variable | QRS Duration (ms) ≤120 (n = 56) | 120–150 (n = 33) | ≥150 (n = 34) | P Value |
|---|---|---|---|---|
| Age (mean±SD, years) | 55 ± 16 | 55 ± 14 | 56 ± 16 | 0.95 |
| Male/female ratio (n) | 45/11 | 21/12 | 25/9 | 0.22 |
| Etiology, n (%) | | | | 0.71 |
| Ischemic | 37 (66%) | 15 (45.5%) | 24 (70%) | |
| Primary dilated | 19 (34%) | 18 (55.5%) | 10 (30%) | |
| QRS duration (ms) | 103 ± 14 | 138 ± 8 | 170 ± 13 | – |
| PR interval (ms) | 182 ± 33 | 199 ± 21 | 200 ± 27 | 0.003 |
| QRS configuration, n (%) | | | | 0.000 |
| LBBB | 23 (41%) | 20 (61%) | 26 (76%) | |
| RBBB | 10 (18%) | 10 (30%) | 6 (18%) | |
| Nonspecific IVCD | 23 (41%) | 3 (9%) | 2 (6%) | |
| NYHA class, n (%) | | | | 0.48 |
| Class III | 49 (87.5%) | 28 (85%) | 26 (76.5%) | |
| Class IV | 7 (12.5%) | 5 (15%) | 8 (23.5%) | |

**Table II.**

Echocardiographic Characteristics of Patients According to Three QRS Groups

| Variable | QRS Duration (ms) ≤120 (n = 56) | 120–150 (n = 33) | ≥150 (n = 34) | P Value |
|---|---|---|---|---|
| LVEF (mean ± SD, %) | 20 ± 7.0 | 19 ± 6.0 | 18 ± 5.0 | 0.40 |
| LVESV (mL) | 154 ± 62 | 142 ± 62 | 179 ± 56 | 0.04 |
| LVEDV (mL) | 199 ± 67 | 188 ± 72 | 222 ± 62 | 0.11 |
| IVMD (ms) | 35 ± 21 | 42 ± 22 | 53 ± 21 | 0.001 |
| PPEP (ms) | 101 ± 50 | 107 ± 35 | 113 ± 75 | 0.26 |
| APEP (ms) | 113 ± 55 | 117 ± 32 | 137 ± 71 | 0.03 |
| Maximal delta-Ts (ms) | 80 ± 28 | 92 ± 43 | 110 ± 28 | 0.000 |

LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVEDV = left ventricular end-diastolic volume; IVMD = interventricular mechanical delay; PPEP = pulmonary pre-ejection period; APEP = aortic pre-ejection period.

around the identity line was seen (Fig. 2). In Group 1 and in Group 2 patients, the latest activated segment was the basal posterior segment in 26.4% and 24.1% of cases, respectively. In Group 3 patients, the latest activated segment was the basal lateral segment in 25.0% of cases (Table III). The area of latest mechanical activation was predominantly located in the lateral and posterior walls (34% and 34%, respectively) in patients with nonischemic dilated cardiomyopathy, whereas in those with ischemic cardiomyopathy, it was more spread over all segments, with most of latest activation situated in the posterior (36%), lateral (23%), and anterior (23%) segments. Etiology of heart failure, age, gender, and NYHA class were similar in patients with and without intraventricular dyssynchrony (all $P > 0.05$). On the contrary, LBBB was observed in the 67% of patients with intraventricular dyssynchrony compared with 45% of patients with no significant intraventricular dyssynchrony ($P = 0.015$). There were also no significant differences in ejection fraction (19.0 ± 6.0% vs. 19.3 ± 7.0%, $P = 0.68$) and left ventricular volumes (LV end-diastolic volume: 208 ± 68 mL vs. 195 ± 69 mL, $P = 0.27$; LV end-systolic volume: 162 ± 60 mL vs. 153 ± 62 mL, $P = 0.42$) between the patients with and without intraventricular dyssynchrony.

### Correlation Between Interventricular and Intraventricular Dyssynchrony

Interventricular dyssynchrony was found in 78% of patients with intraventricular dyssynchrony whereas 20% of patients without intra-

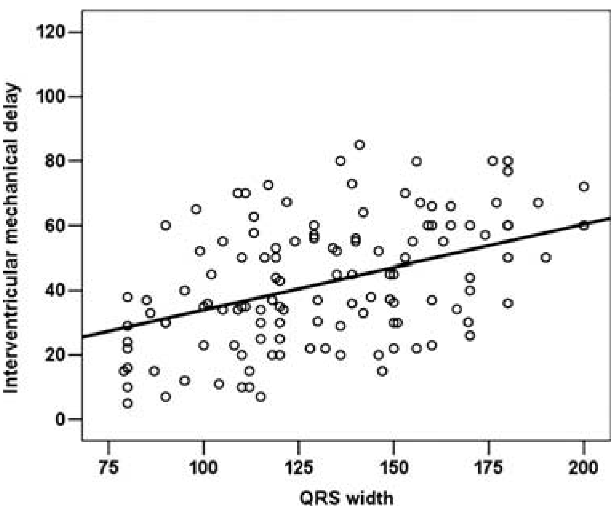


**Figure 1.** *Relationship between IVMD (ms) and QRS duration ($Y = 0.26X + 7.6$, $n = 123$, $r = 0.56$, $P < 0.000$).*

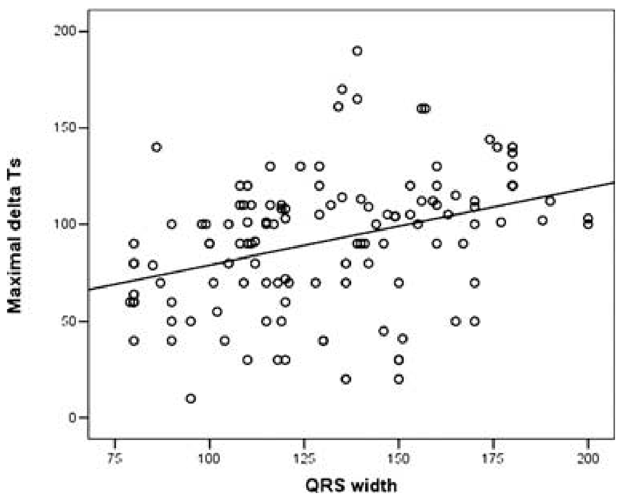


**Figure 2.** *Relationship between intraventricular mechanical delay (maximal delta-Ts) and QRS duration ($Y = 0.4X + 39$, $n = 123$, $r = 0.35$, $P < 0.000$).*

**Table III.**

Most Delayed Segments in Three QRS Groups

| | QRS Duration (ms) | | |
|---|---|---|---|
| Variable | ≤120 (n = 56) | 120–150 (n = 33) | ≥150 (n = 34) |
| Basal anterior segment (%) | 11.3 | 17.3 | 7.1 |
| Mid anterior segment (%) | 11.3 | 3.4 | 10.7 |
| Basal septal segment (%) | 0 | 3.4 | 0 |
| Mid septal segment (%) | 0 | 0 | 7.1 |
| Basal anteroseptal (%) | 0 | 0 | 0 |
| Mid anteroseptal (%) | 0 | 0 | 0 |
| Basal posterior segment (%) | 26.4 | 24.1 | 17.9 |
| Mid posterior segment (%) | 13.2 | 10.3 | 10.7 |
| Basal lateral segment (%) | 7.5 | 13.8 | 25.0 |
| Mid lateral segment (%) | 13.3 | 13.8 | 14.3 |
| Basal inferior segment (%) | 5.7 | 3.5 | 3.6 |
| Mid inferior segment (%) | 11.3 | 10.4 | 3.6 |

ventricular dyssynchrony also had interventricular dyssynchrony (Pearson correlation: 0.58, $P < 0.000$). This correlation increased in parallel to the QRS duration (Pearson correlation: 0.44 and $P = 0.001$ in Group 1; Pearson correlation: 0.75 and $P = 0.000$ in Group 3), so that 93% of Group 3 patients with intraventricular dyssynchrony also had interventricular dyssynchrony; among Group 2 and Group 1 patients with intraventricular dyssynchrony, interventricular dyssynchrony was observed in 75% and 60% of patients, respectively.

## Discussion

The main findings of the present study are as follows:

1. Interventricular and intraventricular dyssynchrony is common in heart failure patients with QRS duration >120 ms;
2. Among heart failure patients with QRS duration >120 ms, 21–42% do not exhibit significant intraventricular dyssynchrony that may explain the lack of response to CRT;
3. A substantial proportion (36%) of heart failure patients with narrow QRS duration exhibit significant intraventricular dyssynchrony and may be candidates for biventricular pacing;
4. There is a good correlation between interventricular and intraventricular dyssynchrony in heart failure patients with QRS duration >150 ms;
5. LBBB is more likely to be associated with significant intraventricular dyssynchrony than other types of intraventricular conduction defect;
6. There are also significant differences between patients with ischemic and nonischemic cardiomyopathies in terms of regional mechanical dyssynchrony.

The response to CRT was initially considered to result in part from resynchronization of interventricular dyssynchrony. Thus patients with interventricular dyssynchrony were selected for CRT. This selection was based on the QRS duration, because this parameter is considered to reflect interventricular dyssynchrony. Indeed, Ghio et al.[15] and Rouleau et al.[20] demonstrated a good relation between interventricular dyssynchrony and QRS duration. Our study also confirmed the good correlation between interventricular dyssynchrony and QRS width. These observations tend to support the use of the QRS duration for patient selection. However, the result of many CRT studies indicated that 20–30% of patients failed to respond to CRT, despite prolonged QRS duration.

Except for the patients with very wide spontaneous QRS complex, mechanical intraventricular dyssynchrony is not necessarily related to electrical dyssynchrony judged by QRS duration. Indeed, the correlation is weak, as we demonstrated in the present study. Some patients with a wide QRS and a severely depressed LVEF may show no area of substantial mechanical delay. This may explain why 20–30% of the patients in the major trials did not have a response to CRT. To date, two studies evaluated the role of the QRS complex as a marker of mechanical LV dyssynchrony.[12,15] In the study of Bleeker et al.[12] severe intraventricular dyssynchrony (defined as septal-to-lateral delay >60 ms) was observed in 27% of the patients with a narrow QRS complex (<120 ms), in 60% of patients with a QRS duration 120–150 ms, and in 70% of patients with QRS ≥ 150 ms. Ghio et al.[15] confirmed the absence of intraventricular dyssynchrony (defined as presence of one or more differences > 50 ms among the regional pre-ejection periods) in 43% of patients with an intermediate QRS duration (120–150 ms) and in 29% of patients with a wide (>150 ms) QRS complex. In our study, substantial intra-LV dyssynchrony on TDI was present in 36% of patients with narrow QRS complex (<120 ms), 58% of patients with intermediate QRS duration (between 120 and 150 ms), and 79% of patients with wide QRS complex (>150 ms). Compared with the aforementioned studies, a slightly higher incidence of intra-LV dyssynchrony in our patients with narrow QRS duration (≤120 ms) and also the patients with wide QRS duration (≥150 ms) may have been related to patient characteristics or definition of intraventricular dyssynchrony. However, 20–40% of patients with heart failure and QRS duration >120 ms do not exhibit intraventricular dyssynchrony, which may explain nonresponse to CRT.

Our study confirmed previous publications regarding global intraventricular dyssynchrony in patients with ischemic versus nonischemic dilated cardiomyopathies.[15,21] However, there are significant discrepancies in the area of latest mechanical activation (regional dyssynchrony) in different studies.[21–23] We observed that, in patients with nonischemic cardiomyopathy, the latest activated areas were mainly located in the lateral and posterior walls of the left ventricle, whereas in those with ischemic cardiomyopathy, the area of latest mechanical activation is not necessarily the lateral wall. This is in accord with the results of the Belgian Multicenter Registry on Dyssynchrony.[21] In a small Group of patients with nonischemic cardiomyopathy and LBBB, Ansalone et al.[22] used pulse-wave Doppler TDI to show the latest activated region tended to be located in the lateral wall (35%). Using three-dimensional echocardiography and tissue tracking, Sogaard et al.[23] reported the lateral and posterior walls of the left ventricle as the predominant myocardial segments with the latest activation in a small number of patients with nonischemic cardiomyopathy.

Previous TDI studies in heart failure patients indicated that in about one third of cases the lateral wall was the latest activated segment in patients with QRS duration above 120 ms.[15,21–23] Similar results were also obtained in our study. However, narrow QRS patient groups were not delayed in the same left ventricular areas in these studies. Ghio et al.[15] reported the medium anterior segment as the predominant delayed site in patients with narrow QRS intervals and the medium lateral segment in those with wide QRS intervals. In contrast, we found that the delayed site was more frequent in the basal posterior in patients with narrow QRS intervals, and in the basal posterior and lateral segments in those with wide QRS intervals. This discrepancy may be explained by differences in patient characteristics or TDI methods used to define regional intraventricular dyssynchrony. These data are indicative of heterogeneity in the sequence of left ventricular activation and wall motion among the heart failure patients with wide QRS intervals. Results of the TDI studies, including the present one, are also in marked contrast to the electrophysiological studies in which the latest site of activation in patients with wide QRS is located in the lateral-posterior left ventricle. In TDI studies, the septum or the anterior or inferior walls are the most delayed sites in a substantial percentage of cases. Potential differences in the area of latest mechanical activation could have practical implications regarding optimal lead positioning. A prospective large-scale study is needed to compare the results of CRT in patients with TDI-guided left ventricular lead placement with those of routine left ventricular lead placement in lateral or posterior cardiac veins.

## Conclusions and Implications

Interventricular and intraventricular dyssynchrony is common in the heart failure patients with QRS duration >120 ms. However, about 20–40% of these patients do not exhibit significant intraventricular dyssynchrony that may explain the lack of response to CRT. On the other hand, a substantial proportion (36%) of heart failure patients with narrow QRS duration show significant intraventricular dyssynchrony and may be considered as potential candidates to CRT.

Among the different types of intraventricular conduction defects, LBBB is more likely to be associated with presence of significant mechanical intraventricular dyssynchrony in TDI. There are also significant differences between patients with ischemic and nonischemic cardiomyopathies in terms of regional mechanical dyssynchrony. This might have implication for coronary sinus lead positioning in biventricular pacing.

## References


1. Bax JJ, Abraham T, Barold SS, Breithardt OA, Fung, JW, Garrigue S, Gorcsan J, et al. Cardiac resynchronization therapy: Part 1. Issues before device implantation. J Am Coll Cardiol 2005; 46:2153–2167.
2. Strickberger SA, Conti J, Daoud EG, Havranek E, Mehra MR, Pina IL, Young J. Council on Clinical Cardiology Subcommittee on Electrocardiography and Arrhythmias and the Quality of Care and Outcomes Research Interdisciplinary Working Group; Heart Rhythm Society. Patient selection for cardiac resynchronization therapy: From the Council on Clinical Cardiology Subcommittee on Electrocardiography and Arrhythmias and the Quality of Care and Outcomes Research Interdisciplinary Working Group, in collaboration with the Heart Rhythm Society. Circulation 2005; 111:2146–2150.
3. Reynolds MR, Joventino LP, Josephson ME. Miracle ICD Investigators. Relationship of baseline electrocardiographic characteristics with the response to cardiac resynchronization therapy for heart failure. Pacing Clin Electerophysiol 2004; 27:1513–1518.
4. Arya A, Haghjoo M, Dehghani MR, Alasti M, Alizadeh H, Kazemi B, Sadr-Ameli MA. Effect of cardiac resynchronization therapy on the incidence of ventricular arrhythmias in patients with an implantable cardioverter-defibrillator. Heart Rhythm 2005; 2:1094–1098.
5. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L. 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.
6. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, et al. Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Investigators. Cardiac Resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Eng J Med 2004; 350:2140–2150.
7. Linde C, Leclercq C, Rex S, Garrigue S, Lavergne T, Cazeau S, McKenna W, et al. Long-term benefits of biventricular pacing in congestive heart failure: Results from the Multisite stimulation in cardiomyopathy (MUSTIC) study. J Am Coll Cardiol 2002; 40:111–118.

8. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, Kocovic DZ, et al. MIRACLE Study Group. Multicenter InSync Randomized Clinical Evaluation. Cardiac resynchronization in chronic heart failure. N Eng J Med 2002; 346:1845–1853.
9. Auricchio A, Stellbrink C, Sack S, Block M, Vogt J, Bakker P, Huth C, et al. Pacing Therapies in Congestive Heart Failure (PATH-CHF) Study Group. Long-term clinical effect of hemodynamically optimized cardiac resynchronization therapy in patients with heart failure and ventricular conduction delay. J Am Coll Cardiol 2002; 39:2026–2033.
10. Molhoek SG, Bax JJ, Boersma E, Van Erven L, Bootsma M, Steendijk P, Van Der Wall EE, et al. QRS duration and shortening to predict clinical response to cardiac resynchronization therapy in patients with end-stage heart failure. Pacing Clin Electrophysiol 2004; 27:308–313.
11. Lecoq G, Leclercq C, Leray E, Crocq C, Alonso C, de Place C, Mabo P, et al. Clinical and electrocardiographic predictors of a positive response to cardiac resynchronization therapy in advanced heart failure. Eur Heart J 2005; 26:1094–1100.
12. Bleeker GB, Schalij MJ, Molhoek SG, Verwey HF, Holman, ER, Boersma E, Steendijk P, et al. Relationship between QRS duration and Left ventricular dyssynchrony in patients with end-stage heart failure. J Cardiovasc Electrophysiol 2004; 15:544–549.
13. Nelson GS, Curry CW, Wyman BT, Kramer A, Declerck J, Talbot M, Douglas MR, et al. Predictors of systolic augmentation from LV preexcitation in patients with dilated cardiomyopathy and intraventricular conduction delay. Circulation 2000; 101:2703–2709.
14. Morris-Thurgood JA, Turner MS, Nightingale AK, Masani N, Mumford C, Frenneaux MP. Pacing in heart failure: Improved ventricular interaction in diastole rather than systolic resynchronization. Europace 2000; 2:271–275.
15. Ghio S, Constantin C, Klersy C, Serio A, Fontana A, Campana C, Tavazzi L. Interventricular and intraventricular dyssynchrony are common in heart failure patients regardless of QRS duration. Eur Heart J 2004; 25:571–578.
16. Yu CM, 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.
17. Leclercq C, Faris O, Tunin R, Johnson J, Kato R, Evans F, Spinelli J, et al. Systolic improvement and mechanical resynchronization does not require electrical synchrony in the dilated failing heart with left bundle-branch block. Circulation 2002; 106:1760–1763.
18. Bax JJ, Ansalone G, Breithardt OA, Derumeaux G, Leclercq C, Schalij MJ, Sogaard P, et al. Echocardiographic evaluation of cardiac resynchronization therapy: Ready for routine clinical use. A critical appraisal. Cardiac resynchronization therapy. J Am Coll Cardiol 2004; 44:1–9.
19. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Klein W, et al. CARE-HF study Steering Committee and Investigators. The CARE-HF study (Cardiac resynchronization in heart failure study): Rationale, design and end points. Eur J Heart Fail 2001; 3:481–489.
20. Rouleau F, Merheb M, Geffroy S, Berthelot J, Chaleil D, Dupuis JM, Victor S, et al. Echocardiographic assessment of the interventricular delay of activation and correlation to the QRS width in dilated cardiomyopathy. Pacing Clin Electrophysiol 2001; 24:1500–1506.
21. Van de Veire N, De Sutter J, Van Camp G, Vandervoot P, Lancellotti P, Cosyns B, Unger P, et al. Belgian Multicenter Registry on Dyssynchrony. Global and regional parameters of dyssynchrony in ischemic and nonischemic cardiomyopathy. Am J Cardiol 2005; 95:421–423.
22. Ansalone G, Giannantoni P, Ricci R, Trambaiolo P, Fedele F, Santini M. Doppler myocardial imaging to evaluate the effectiveness of pacing sites in patients receiving biventricular pacing. J Am Coll Cardiol 2002; 39:489–499.
23. Sogaard P, Egeblad H, Pedersen A, Kim WY, Kristensen BO, Hansen PS, Mortensen PT. Sequential versus simultaneous biventricular resynchronization fro severe heart failure. Evaluation by tissue Doppler imaging. Circulation 2002; 106: 2078–2084.