Correlation between Electrocardiographic Features and Mechanical Dyssynchrony in Heart Failure Patients with Left Bundle Branch Block

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Background: Few electrocardiographic parameters beyond the QRS duration were studied with regard to the correlation with mechanical dyssynchrony. This study aims to analyze the correlation between electrocardiographic parameters and mechanical dyssynchrony in patients with symptomatic heart failure (HF) and left bundle branch block (LBBB).

Methods: Patients with HF, ejection fraction $\leq 35\%$, and QRS interval ≥ 120 ms with a LBBB were prospectively studied.

We analyzed the correlation between electrocardiographic parameters (QRS duration, R voltage in limb leads, S voltage in precordial leads, Sokolow and Cornell indexes, QRS axis deviation, and QRS notches in lateral and inferior leads) and mechanical dyssynchrony measured by tissue Doppler imaging (TDI).

Results: A group of 50 patients were studied, 60% male, 78% with nonischemic cardiomyopathy, NYHA Class III–IV (86%), and ejection fraction of 0.22 ± 0.6 . Intra- and interventricular dyssynchrony occurred in 68% and 74% of patients, respectively. The S amplitude in precordial leads and the Sokolow and Cornell indexes show a weak correlation with the degree of dyssynchrony.

In the patients with QRS notching in the lateral and inferior leads, we observed significantly greater prevalence of intraventricular dyssynchrony, with sensitivity and specificity of 85% and 56%, respectively, for notches in lateral leads.

The QRS duration presents moderate correlation with the degree of both intraventricular ($r = 0.48$) and interventricular dyssynchrony ($r = 0.46$).

Conclusion: The following electrocardiographic parameters were related to the degree of mechanical dyssynchrony: QRS duration and notches in QRS. In addition, the patients tend to have highest S amplitude in precordial leads.

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Intraventricular conduction disorder with wide QRS complex, especially left bundle branch block (LBBB) occurs in 20–35% of patients with systolic heart failure (HF) and is associated with cardiac dyssynchrony and higher risk for adverse events.^{1,2} Cardiac resynchronization therapy (CRT) is indicated for patients with advanced HF, class III and IV, and ejection fraction (LVEF) $< 35\%$, refractory to medical treatment and QRS interval ≥ 120 ms.³ Large randomized trials have clearly demonstrated

the beneficial effects of CRT in the patients with this profile including mortality reduction.^{4,5}

However, about 30% of patients undergoing CRT, selected on the basis in the current criteria do not show improvement in symptoms and, as much as 40–50% of the patients do not show improvement in echocardiographic parameters.^{4–6}

The main mechanism responsible for the benefits by the CRT is the reduction of electrical and mechanical dyssynchrony.⁷ The mechanical

dyssynchrony has been evaluated by imaging methods such as echocardiography and tagged magnetic resonance imaging.⁸⁻¹⁰

Few electrocardiographic parameters beyond the QRS duration were studied with regard to the correlation with mechanical dyssynchrony. Several echocardiographic studies have shown that QRS duration is not a good marker of mechanical dyssynchrony.^{11,12}

This study aims to analyze the correlation between electrocardiographic parameter and mechanical dyssynchrony in patients with HF and a LBBB.

METHODS

Patients

In this prospective study, we selected patients that are candidates for resynchronization therapy, who have symptomatic HF, ejection fraction less than or equal to 35%, and QRS interval ≥ 120 ms on the electrocardiogram, with a pattern of LBBB. We excluded patients with nonsinus rhythm, with coronary syndrome, and permanent pacemaker. Patients were selected based on symptoms and signs of HF and previously conducted tests (ECG, echocardiography), and sent to perform 12-lead electrocardiogram and an echocardiogram to assess dyssynchrony.

Patients were evaluated at the Onofre Lopes Hospital in the period from November 2008 to December 2009. This study was approved by the ethics committee of the University and a written informed consent was obtained from all patients.

Electrocardiograms

Standard 12-lead electrocardiograms were acquired at a paper speed of 25 mm/s and a scale of 10 mm/mV with the patient in the supine position.

The parameters were evaluated by two cardiologists, blinded to the clinical condition of patients and the results of echocardiograms.

The electrocardiograms were performed by an experienced technician with special attention to the chest landmarks of the precordial leads.

LBBB was characterized by following criteria: QRS duration ≥ 120 ms; rS or QS in V_1 and V_2 and a broad and notched or slurred R wave in leads I, V_5 or V_6 .

The following parameters were evaluated manually traced with the aid of a magnifying glass, as defined below:

QRS duration: defined as the maximal duration of the QRS complex in any of the 12 leads, measured from the earliest onset of the QRS complex to the point where the QRS complex returned to baseline. The QRS duration was measured in milliseconds.

QRS axis: determined in the frontal plane through the hexaxial system leads. Axis left deviation (frontal plane) was considered when ≥ -30 degrees and right axis deviation when $\geq +90$ degrees.

Voltage measurements: the following voltage measurements were considered for analysis:

- Maximum R in limb leads: The tallest R wave in any of the standard limb leads.
- Maximum S wave in chest leads: the S wave of greater amplitude in the horizontal plane.
- S wave in V_1 , V_3 , and V_4 .
- R wave in V_5 or V_6 (whichever is larger).
- Sokolow-Lyon Index: sum of S V_1 + R V_5 or V_6 .
- Cornell-voltage Index: sum of S V_3 + R aVL.

QRS notch in the inferior leads: defined as the record of notches in the R or S wave of QRS complex in at least two of the inferior leads (II, III and aVF). **QRS notch in lateral leads:** notches in the QRS in leads that look to the ventricle (I, aVL, V_5 , V_6) in at least two of these leads.

The amplitude measures were taken in millimeters (mm).

Standard Echocardiography

Echocardiographic examinations were performed by a single operator using a commercial ultrasonographic machine (Invasor C HD, Philips Medical Systems, Andover, MA), with the use of a 3.5 MHz transducer and an electrocardiographic signal of good quality. Examination M-mode and two-dimensional were recorded and the measurements were taken according to the American Society of Echocardiography in conjunction with the European Society of Echocardiography.¹³ Left ventricular end-systolic and diastolic dimensions and volumes and left ventricular ejection fraction were calculated using the biplane Simpson's technique.

Assessment of Mechanical Dyssynchrony

The color tissue Doppler image (TDI) was used to obtain views of the basal segment of the septal, lateral, anterior and inferior LV plane (apical four- and two-chamber), and the free wall of the right ventricle (apical four-chamber). The electromechanical delay was defined as the time between the beginning of the QRS complex of the electrocardiogram and the peak systolic wave measured by Doppler. Measurements were obtained from the average of three measurements, made at the end of expiration.^{9,14}

The aortic preejection time was measured from the beginning of QRS complex to the beginning of the aortic flow velocity recorded by pulsed-wave Doppler in apical five-chamber view. The pulmonary preejection time was determined from the onset of QRS to the onset of pulmonary flow velocity curve recorded in the left parasternal view.¹⁵ The difference between the two values determined the interventricular mechanical delay.

Intraventricular dyssynchrony was characterized by the activation delay between the left ventricle (LV) segments by TDI according to the following criteria: difference in electromechanical interval between two opposing wall of the LV ≥ 65 ms by TDI, a delay that predicted a favorable clinical response and LV reverse remodeling.¹⁴

Interventricular dyssynchrony was based on two indices: (1) the delay between the free wall of the right ventricle and the maximum value of the LV ≥ 60 ms by TDI and (2) the interventricular mechanical delay > 40 ms by pulsed Doppler.¹⁵ When there was disagreement between these methods (tissue Doppler and pulsed Doppler), we considered the result of TDI to characterize interventricular dyssynchrony.

Statistical Analysis

Analyses were performed with MedCalc version 11.1.1.0 (MedCalc Software, Mariakerke, Belgium). Continuous variables were expressed as means $\pm$ standard deviation and categorical data as relative frequency. Comparative analysis between groups (e.g., with and without dyssynchrony) were realized by the Mann-Whitney U-test. Differences between categorical variables were evaluated by means of the chi square test. The correlation to analyze the degree of association between two variables was made by the calculation of the Pear-

son coefficient (r). Since intra- and interventricular dyssynchrony measurements are not normally distributed, we applied a log transformation.

Variables with a P value of ≤ 0.20 on univariate analysis were subsequently included in the corresponding stepwise multivariate analysis to determine the associations between the studied variables and dyssynchrony indexes, adjusted for other confounders. The agreement between the measurements performed by two observers (S voltages) in a same ECG tracing was determining by calculus of the concordance correlation coefficient. Two-tailed P values < 0.05 were retained for statistical significance.

RESULTS

Patient Characteristics

A total of 50 patients were studied, 78% presenting nonischemic cardiomyopathy (only one had Chagas' disease). Most of these patients subsequently underwent implantation of biventricular pacemaker.

The baseline characteristics of patients are presented in Table 1.

Reproducibility of Electrocardiographic Measurements

There was concordance between the two observers in 94% and 96% of cases, respectively, for the presence of notches in the QRS in the inferior and lateral leads. The concordance correlation coefficient was 0.95 (0.92–0.97) and 0.97 (0.94–0.99) for measurements of voltages of the S wave in V_1 and V_3 , respectively.

Prevalence of Mechanical Dyssynchrony

Among the patients studied, 34 (68%) presented with intraventricular dyssynchrony by tissue Doppler.

Table 1. Baseline Characteristics of the Patients

Parameter	Value
Age (yrs)	60.0 $\pm$ 11.7
Men/woman	30/20
Nonischemic etiology	78%
NYHA class III/IV	86%
LV end-diastolic diameter (mm)	69.9 $\pm$ 11.2
LV end-systolic diameter (mm)	62.2 $\pm$ 11.7
LV ejection fraction (%)	22.3 $\pm$ 6.4

Table 2. Correlation (R) between the QRS Duration and Voltage Measurements with the Degree of Dyssynchrony by Tissue Doppler (TDI)

Parameter (ECG)	Intra-V D (r)	P	Inter-V D (r)	P
QRS duration (ms)	0.48	<0.001	0.46	<0.001
Maximum R in limb leads (mm)	-0.06	0.74	0.04	0.80
R wave in aVL (mm)	0.03	0.86	0.10	0.60
S wave in V ₁ (mm)	0.31	0.028	0.15	0.31
S wave in V ₃ (mm)	0.35	0.013	0.33	0.05
S wave in V ₄ (mm)	0.32	0.037	0.30	0.04
Maximum S in chest leads	0.36	0.01	0.28	0.28
R wave in V ₅ or V ₆ (mm)	0.23	0.13	0.16	0.28
Cornell index (mm)	0.30	0.037	0.33	0.02
Sokolow index (mm)	0.32	0.027	0.19	0.18

Intra-V D = intraventricular dyssynchrony; Inter-V D = interventricular dyssynchrony; r = Pearson coefficient.

There was an agreement between echocardiographic methods (pulsed Doppler and tissue Doppler) in the diagnosis of interventricular dyssynchrony in 92% of the cases.

Interventricular dyssynchrony occurred in 37 patients (74%), while both intraventricular and interventricular dyssynchrony was observed in 32 of 50 patients (64%).

Relationship between ECG Parameters and Intraventricular Dyssynchrony

We observed a correlation between the amplitude of the S wave in precordial leads (S wave in V₁, V₃, V₄, and maximum S wave in chest leads) and the indexes of Sokolow-Lyon and Cornell with the degree of intraventricular dyssynchrony by tissue Doppler. However, the correlation between voltage and dyssynchrony was weak (Table 2).

In the patients with QRS notching in the lateral and inferior leads, there was significantly greater

prevalence of intraventricular dyssynchrony by tissue Doppler (Table 3). The presence of notches in lateral leads was associated with intraventricular dyssynchrony, with high sensitivity (85%) and high positive predictive value (81%), whereas the specificity and the negative predictive value were 56% and 64%, respectively. The notches in the QRS were generally observed in several leads in patients with increased intraventricular dyssynchrony.

The mean of QRS duration in patients with notches was significantly greater than in patients without notches. However, the notches in the lateral leads are related to a greater degree of intraventricular dyssynchrony, regardless of QRS duration. In a multiple regression model, including several variables (ejection fraction, QRS width, maximum S in chest leads, and notches in lateral leads), the QRS duration (P = 0.01), maximum S (P = 0.04), and notches in lateral leads (P = 0.03) presents correlation with degree of intraventricular

Table 3. Comparative Analysis of Patients with and without Intraventricular Dyssynchrony by Tissue Doppler

Parameter (ECG)	With Dyssynchrony (n = 34)	Without Dyssynchrony (n = 16)	P
QRS duration (ms)	160 (160–180) ^a	140 (126–160)	0.003
R wave in aVL	6.5 (4.6–8.9)	7.0 (3.7–9.7)	0.12
Maximum S in chest leads	30.5 (26.8–32)	23.5 (16.0–30.2)	0.024
S wave in V ₁ (mm)	17 (12.9–19.2)	8.5 (6–11.4)	0.004
S wave in V ₃ (mm)	25 (20.9–31)	21.5 (11.9–26.4)	0.06
S wave in V ₄ (mm)	17.5 (12.6–25.6)	11 (4.3–17.7)	0.022
R wave in V ₅ or V ₆ (mm)	8.5 (6–12)	5 (3.9–6.5)	0.037
Cornell index (mm)	32 (26.5–38.1)	27 (17.8–38.6)	0.14
Sokolow index (mm)	25.5 (21.6–31.2)	12 (9.9–21.2)	0.004
QRS axis deviation	50%	56%	0.93
QRS notches in II-III-aVF (%)	79%	37%	<0.001
QRS notches in lateral leads	85%	44%	<0.001

^aMedian and 95% Confidence Interval (CI) for the median (Mann-Whitney test).

Figure 1. ECG of a patient with dilated cardiomyopathy, exhibiting typical notches in lateral (I; aVL and V₅) and inferior leads (III; aVF) associated with S waves in precordial leads V₁ to V₃. The QRS duration is 160 ms. Tissue Doppler images showed significant intraventricular and interventricular dyssynchrony (intraventricular delay = 100 ms; interventricular delay = 120 ms).

dyssynchrony (multiple correlation coefficient = 0.68, $P < 0.001$).

We found no correlation between the magnitude of R waves in limb leads and mechanical dyssynchrony. There was also no relation between axis deviation and intraventricular dyssynchrony.

The group with intraventricular dyssynchrony has a higher frequency of notches in the lateral and inferior leads, longer QRS duration, and higher S voltage in the horizontal plane (Figs. 1–3).

Relationship between ECG Parameters and Interventricular Dyssynchrony

The correlation between QRS width and S amplitude with the degree of interventricular dyssynchrony by TDI method is shown in Table 2. Similarly to that observed with intraventricular dyssynchrony, the group with interventricular dyssynchrony showed a higher prevalence of notches in the QRS: present in lateral leads in 92%

Figure 2. The ECG shows intraventricular conduction delay with QRS of 130 ms. Absence of notches in the QRS and deep S waves in precordial leads. There is no mechanical dyssynchrony by TDI (intraventricular delay = 30 ms; interventricular delay = 20 ms).

Figure 3. The ECG shows notches in II, III, aVF, aVL, V₅, and V₆. QRS duration = 140 ms. Patient with heart failure and intra- and interventricular dyssynchrony.

of patients with interventricular dyssynchrony and only 31% of those without dyssynchrony ($P < 0.001$). The group with interventricular dyssynchrony by TDI also has a higher voltage of S in chest leads (maximum S wave = 30 [25–31] vs 21.5 [14.5–30.5], $P = 0.02$) and higher Cornell index: 32 (29.6–37.6) versus 22.7 (17–33); $P = 0.02$ in relation to the group without interventricular dyssynchrony.

The QRS width has moderate correlation with the degree of the interventricular mechanical delay by pulsed Doppler ($R = 0.50$, $P < 0.001$). We also observed increased prevalence of notches in the QRS in patients with interventricular dyssynchrony (defined as interventricular mechanical delay > 40 ms), compared to the patients without dyssynchrony: QRS notches were found in the lateral leads in 32 of 36 (89%) patients with interventricular dyssynchrony by pulsed Doppler and in only four of 14 (29%) patients without dyssynchrony ($P < 0.001$). Moreover, there was no correlation between the measure of voltage and the degree of interventricular mechanical delay (example: correlation with largest S wave in the horizontal plane = 0.20, $P = 0.18$).

For TDI, the correlation between electrocardiographic markers and the degree of interventricular or intraventricular dyssynchrony was of similar magnitude for most parameters (Table 2), as well as the relationship between the presence of notches in the QRS and the record of interventricular or intraventricular dyssynchrony.

DISCUSSION

The main finding of this study is that in addition to QRS duration, the amplitude of the S wave in precordial leads and the presence of notch on the R or S in the lateral and inferior leads were correlated with the degree of mechanical dyssynchrony measured by tissue Doppler. These parameters are easy to evaluate in the standard 12-leads ECG. However, as observed with the QRS duration, the correlation between S voltages in horizontal plane and dyssynchrony indices was weak.

The correlation between electrical dyssynchrony, as measured by QRS duration and mechanical dyssynchrony varies among studies, with the majority showing a weak or moderate relationship between QRS duration and degree of dyssynchrony.^{11,12,16,17} Tornoux et al.¹⁷ observed correlation between QRS duration and interventricular dyssynchrony ($r = 0.37$) and intraventricular dyssynchrony ($r = 0.47$) only in the group with chronic nonischemic etiology.

The variable proportion of ischemic and nonischemic could explain the discrepancies between studies, as well as the different methods used to assess mechanical dyssynchrony. In our study, there was a predominance of nonischemic cardiomyopathy (78% of cases) and noticed the tie in between QRS duration and degree of intraventricular ($r = 0.48$) and interventricular dyssynchrony ($r = 0.46$), with values near the above study for patients with nonischemic etiology.

Strauss et al.,¹⁸ basing on activation studies and computer models, concluded that the endocardial

activation time in the classic left bundle block is about 140–150 ms, which is the sum of septal activation (40 ms) plus 50 ms to propagate and activate the anterossuperior and inferior walls plus 50 ms to activate the posterolateral wall of the LV. The association of left ventricular hypertrophy (LVH) in addition increases the duration of QRS. Das et al.¹⁹ showed that the QRS duration in LBBB is an inverse relationship with the ejection fraction, and QRS $\geq$ 170 ms a marker of ventricular dysfunction.

Therefore, ventricular hypertrophy and enlargement of the highest intensity, which would be translated by both increased QRS voltage and QRS duration, would be related to the degree of dyssynchrony.

Broad, notched R waves in leads I, aVL, and lateral precordial are a common diagnostic criteria for classical complete LBBB.²⁰

The occurrence of notches in the QRS (R or S waves) in the lateral (I, aVL, V₅, V₆) and/or inferior leads is a frequent finding in LBBB associated with nonischemic or ischemic cardiomyopathy. In our study, this aspect was observed in 72% and 64% of patients in lateral and inferior leads, respectively.

The presence of notches in the QRS, or in the inferior or lateral leads was more frequent in patients with intraventricular dyssynchrony.

A recent study of Sweeney et al.²¹ showed that the surface ECG use accurately predicts LV reverse remodeling after CRT. Greater longest LV activation time, smaller scar volume (calculated by Selvester score for LBBB) in the baseline ECG, and evidence of wavefront fusion on the paced ECG anticipate higher probability of reverse remodeling. The LV activation time was measured using QRS notches that indicate the transition between RV and LV activation time.

Moreover, the fragmented QRS complexes in resting ECG were associated with significant intraventricular dyssynchrony in patients with non-ischemic cardiomyopathy, narrow QRS, and sinus rhythm. The presence of fragmented QRS complexes in leads corresponding to the specific ventricular segment in basal ECG was found to detect intraventricular dyssynchrony with 90.6% sensitivity and negative predictive value of 85%.²²

Notches in QRS during LBBB may occur because of myocardial scar, especially multiple notches and in the first 40 ms of the S wave in V₁ through V₂.¹⁸ The value of notches in the ascending portion of the S wave in leads V₃–V₄ to diagnostic of anterior myocardial infarction has been emphasized many

years ago by Cabrera et al.²³ We consider in our study only the presence of notches in the inferior and lateral leads.

There was no association between axis deviation and intraventricular or interventricular dyssynchrony in our study. Instead, Fauchier et al.,¹⁶ using phase analysis of equilibrium radionuclide angiography, observed that patients with LBBB on the left axis had the highest degree of intraventricular dyssynchrony compared to patients with LBBB on the normal axis (intra-LV dyssynchrony in 92% and 46% of patients, respectively).

In conclusion, we observed that in patients with HF and LBBB pattern, the following abnormalities in the standard 12-lead ECG were related to the degree of mechanical dyssynchrony assessed by Tissue Doppler Echocardiography: QRS duration and notches in QRS. In addition, the patients tend to have highest S waves amplitude in the horizontal plane.

Limitations

A limitation of this study is the method used to assess mechanical dyssynchrony. The best method to assess the mechanical dyssynchrony has been the subject of controversy. The method used for assessment of intraventricular dyssynchrony is a TDI parameter examining the time to peak systolic contraction between two myocardial segments. Although the single-study center have reported relationships between echocardiographic measurements and outcomes after CRT,^{8,9,14} the multicenter PROSPECT trial²⁴ demonstrated that the mechanical dyssynchrony indexes presents modest sensitivity and specificity to distinguish responders from nonresponders to CRT.

Another limitation concerns the low reproducibility of the amplitudes and of the precordial leads due to variations in the electrodes's position on the chest between a series of electrocardiograms.²⁵ This can affect the voltage of the precordial leads. Nevertheless, indices using precordial leads as the Sokolow, are accepted criteria for diagnosis of LVH.

REFERENCES

1. Xiao HB, Roy C, Fujimoto S, et al. Natural history of abnormal conduction and its relation to prognosis in patients with dilated cardiomyopathy. *Int J Cardiol* 1996;53:163–170.
2. Baldasseroni S, Opasich C, Gorini M, et al.; Italian Network on Congestive Heart Failure Investigators. Left

- bundle-branch block is associated with increased 1-year sudden and total mortality rate in 5517 outpatients with congestive heart failure: A report from the Italian network on congestive heart failure. *Am Heart J* 2002;143:398-405.
3. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: A report of the ACC/AHA task force on practice guidelines. *Circulation* 2008;117:e350-e408.
4. Abraham WT, Fisher WG, Smith AL, et al for the Multicenter InSync Randomized Clinic Evaluation (MIRACLE). Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;346:1845-1853.
5. Cleland JGG, Daubert J-C, Erdmann E, et al 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.
6. Reuter S, Garrigue S, Barold SS, et al. Comparison of characteristics in responders versus nonresponders with biventricular pacing for drug resistant congestive heart failure. *Am J Cardiol* 2002;89:346-350.
7. Porciani MC, Macioce R, Demarchi G, et al. Effects of cardiac resynchronization therapy on the mechanisms underlying functional mitral regurgitation in congestive heart failure. *Eur J Echocardiogr* 2006;7:31-39.
8. Yu CM, Chau E, Sanderson JE, et al. Tissue Doppler echocardiographic evidence of reverse remodeling and improve synchronicity by simultaneously delaying regional contraction after biventricular pacing therapy in heart failure. *Circulation* 2002;105:438-445.
9. Bleeker GB, Mollema SA, Holman ER, et al. Left ventricular resynchronization is mandatory for response to cardiac resynchronization therapy: Analysis in patients with echocardiographic evidence of left ventricular dyssynchrony at baseline. *Circulation* 2007;116:1440-1448.
10. Bilchick KC, Dimaano V, Wu KC, et al. Cardiac magnetic resonance assessment of dyssynchrony and myocardial scar predicts function class improvement following cardiac resynchronization therapy. *J Am Coll Cardiol Img* 2008;1:561-565.
11. Emkanjoo Z, Esmailzadeh M, Mohammad Hadi N, et al. Frequency of inter- and intraventricular dyssynchrony in patients with heart failure according to QRS width. *Eurpace* 2007;9:1171-1176.
12. Bleeker GB, Schalij MJ, Molhoek SG, et al. Relationship between QRS duration and left ventricular dyssynchrony in patients with end-stage heart failure. *J Cardiovasc Electrophysiol* 2004;15:544-549.
13. Lang RM, Biering M, Devereux RB, et al. Recommendations for chamber quantification: A report from the American Society of Echocardiography, guidelines and standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a Branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440-1463.
14. Bax JJ, Bleeker GB, Marwick TH, et al. Left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronization therapy. *J Am Coll Cardiol* 2004;44:1834-1840.
15. Rouleau F, Merheb M, Geffroy S, et al. Echocardiographic assessment of the interventricular delay of activation and correlation to the QRS width in dilated cardiomyopathy. *Pacing Clin Electrophysiol* 2001;24:1500-1506.
16. Fauchier L, Marie O, Casset-Senon D. Reliability of QRS duration and morphology on surface electrocardiogram to identify ventricular dyssynchrony in patients with idiopathic dilated cardiomyopathy. *Am J Cardiol* 2003;92:341-344.
17. Tournoux F, Donal E, Leclercq C, et al. Concordance between mechanical and electrical dyssynchrony in heart failure patients: A function of the underlying cardiomyopathy? *J Cardiovasc Electrophysiol* 2007;18:1022-1027.
18. Strauss DG, Selvester RH. The QRS complex—a biomarker that “images” the heart: QRS scores to quantify myocardial scar in the presence of normal and abnormal ventricular conduction. *J Electrocardiol* 2009;42:85-96.
19. Das MK, Cheriparambil K, Bedi A, et al. Prolonged QRS duration (QRS $\geq$ 170 ms) and left axis deviation in the presence of left bundle branch block: A marker of poor left ventricular systolic function? *Am Heart J* 2001;142:756-759.
20. Mirvis DM, Goldberger AL. Electrocardiogram. In: Libby P, Bonow RO, Mann DL, Zipes DP. (eds.) *Braunwalds Heart Disease: A Textbook of Cardiovascular Medicine*, 8th Edition. Philadelphia, PA, Saunders Elsevier, 2008, pp. 1141-1226.
21. Sweeney MO, van Bommel RJ, Schalij MJ, et al. Analysis of ventricular activation using surface electrocardiography to predict left ventricular reverse volumetric remodeling during cardiac resynchronization therapy. *Circulation* 2010;121:626-634.
22. Tigen K, Karaahmet T, Gurel E, et al. The utility of fragmented QRS complexes to predict significant intraventricular dyssynchrony in nonischemic dilated cardiomyopathy patients with a narrow QRS interval. *Can J Cardiol* 2009;25:517-522.
23. Cabrera E, Friedland C. La onda de activación ventricular en el bloqueo de rama izquierda con infarto: Un nuevo signo electrocardiográfico. *Arch Inst Cardiol Mex* 1953;23:441-460.
24. Chung ES, Leon AR, Tavazzi L, et al. Results of the predictors of response to CRT (PROSPECT) trial. *Circulation* 2008;117:2608-2616.
25. Wenger W, Kligfield P. Variability of precordial electrode placement during routine electrocardiography. *J Electrocardiol* 1998;29:179-184.