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Correlation between Right to Left Ventricular Activation Delay with Paced QRS Duration in Cardiac Resynchronization Therapy

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Abstract

Cardiac resynchronization therapy (CRT) is an effective treatment in advanced heart failure (HF). However, almost one third of patients fail to respond to this therapy. We aimed to evaluate the correlation between intrinsic right ventricular (RV) and left ventricular electrogram delay (EGM delay) and corresponding paced QRS duration with narrowing of QRS (delta QRS) after simultaneous biventricular pacing (simul QRS). Fifty-seven consecutive patients who underwent CRT implantation between January 2014 and January 2015 were enrolled. Intrinsic EGM delay, RV only, LV50 pacing QRS width and simul QRS duration were evaluated in 51 surviving patient at 6 months follow-up visit to evaluate the relationship between baseline EGM delay and delta QRS in these different pacing modes and assess its impact on response to CRT. Forty patients (78.4%) were defined as responder. Difference in EGM delay between responder and non-responder patients wasn't significant (69± 36 and 53 ± 37 msec respectively). Correlation between intrinsic delta EGM and simul QRS was not significant in responder and non-responders. Simul QRS showed significant correlation with RV only and LV50 pacing QRS in responders (correlation coefficient: 0.49 and 0.35 respectively). Simul QRS showed significant correlation with RV only and LV50 pacing but not intrinsic QRS duration. These findings indicate that intrinsic EGM delay does not have a strong correlation with QRS narrowing in simul QRS, RV only and LV50 paced methodsin patients with implanted CRT at 6-month follow-up.

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Keywords

Heart failure, Electrogram delay, QRS duration.

Introduction

Cardiac resynchronization therapy (CRT) is an effective treatment for patients with advanced heart failure (HF) and prolonged QRS (Michele Brignole and Gonzalo Baron-Esquivias. 2013). CRT by mechanical and biomedical mechanisms improves contractility and cardiac output of left ventricle (Hana Cho *et al.*, 2012), functional capacity, quality of life of patients and decrease in rate of hospitalization. This therapy can increase survival of HF patients (John Rickard *et al.*, 2011). One of the main problems with CRT device is the issue of non- response which may happen in 30%-35% of patients (Mohamed Loutfi *et al.*, 2016). One of the important criteria for response to CRT is narrowing of QRS after implantation. Factors predicting narrowing of QRS after Biventricular pacing are longer QRS duration, male sex and small age of patients (Frederic A. Sebag *et al.*, 2012). QRS narrowing is related to ventricular remodeling which is important for good response to CRT (John Rickard *et al.*, 2011).

Many studies tried to overcome the issue of non-response, some of those used the ventricular electrograms (EGMs). Left ventricular (LV) EGM and its distance to Q wave in surface ECG evaluated and reported as an independent factor for ventricular remodeling (Michael R. Gold UB-G and Jagmeet P. Singh, 2011). Evaluation of LV lead electrical delay reported to be useful during CRT implantation for better hemodynamic response (Jagmeet P. Singh *et al.,* 2006) and pacing at latest activation site of LV was resulted in better hemodynamic response (Francesco Zanon *et al.*, 2014).

Patients with heart failure (HF) who are candidate for CRT device have wide QRS duration and frequently have left bundle branch block (LBBB) (Michele Brignole and Gonzalo Baron-Esquivias. 2013). In patients with LBBB, electrical activation of ventricles starting from RV and then slowly spreads via the interventricular septum into the lateral wall of the LV. There are heterogeneous endocardial activation of LV in patients with HF and LBBB. Also there are heterogeneous LV endocardial break through which may occur at different septal regions (Marc Strik and Angelo Auricchio, 2012). On the other hand characteristics of fascicles and specialized conduction systems have influences on morphology and duration of QRS (Nina Hakacova *et al.*, 2008). The presence of fibrotic tissue which is seen in ischemic and non-ischemic cardiomyopathies may cause disturbances in conduction velocity and direction of electrical activity of LV (Panfilov, 2007). All of these variations show the presence of complicated LBBB in HF patients that may be the cause of failure in response to CRT in some patients.

The combination of variations and disturbances mentioned above may present as delay in activation of LV which can be measured by difference between RV and LV lead EGM in patients with implanted CRT device. It is also possible to pace RV separately or pace LV with varying difference of LV to RV and vice versa and record resultant electrocardiograms. Because of these possibilities we decided to evaluate the effects of EGM delays on the QRS duration in various pacing modes. As a secondary aim correlation between the QRS duration of simultaneous Biv pacing and other forms of pacing modes evaluated.

Materials and Methods

In a prospective before and after study, from January 2014 to January 2015, 57consecutive patients with HF who were eligible for implanting CRT device were enrolled. Institutional review board of Tabriz University of Medical Sciences approved the study. Inclusion criteria were eligibility for cardiac resynchronization therapy based on 2013 ACC/AHA Guideline for the Management of Heart Failure (Clyde *et al.,* 2013). Patients who were receiving antiarrhythmic medications, and those who had implanted epicedial lead or high threshold LV lead (>2.5 v/0.04 sec) were excluded from the study. A research member approached each patient, and informed consent was obtained upon full description of the study. CRT was implanted with RV lead implanted at RV apex and LV lead in the suitable vein (favorable size and threshold, not apical) in the posterolateral, posterior or anterolateral veins (Jagmeet P. Singh *et al.*, 2011). Ventricular pacing was programed as simultaneous LV to RV pacing. Baseline characteristics including age, sex, presence of cardiac risk factors, type of cardiomyopathy, position of LV lead were collected. QRS and EGM delays were evaluated at six months follow-up. All patients received standard HF therapy at managing cardiologists' discretion during this period. Follow up electrocardiograms (ECGs) was done at 6 months for evaluation of mean 12 leads QRS duration (Mohit K Turagam, 2013). EGM delay was measured from intrinsic deflection of bipolar LV and RV EGMs (Michael R. Gold UB-G and Jagmeet P. Singh, 2011; Marta de Riva-Silva MaL, 2014) by cardio caliper software. All EGMs and ECGs were recorded at speed of 25 mm/sec. One electrocardiograph device (Cardiotouch6.06c.30 from Bionet company with 6 channels recording at speed of 25.0 mm/sec and amplitude of 10.0 mm/mv, filtering: 0.1 Hz – 40 Hz, AC 50 Hz, EMG, with power supply of 220 v and 50 Hz) was used for all patients. The following EGMs and concomitant ECGs obtained: 1- Intrinsic (I) which obtained by programming CRT device to long atriventricular delay (AVD) in patients with good AV conduction or to VVI mode =30 b/min patients with long AV conduction or AV block or atrial fibrillation. In patients with Medtronic devices R sense pacing was turned off temporarily, 2- Simultaneous LV to RV pacing (Simul), 3- RV only pacing, and 5- fifty msec earlier LV to RV (LV 50). The programmed AVD during pacing was 130 msec. Electrocardiograms and EGMs were obtained after 3 minutes of adjusting the mode of pacing. The results were obtained by averaging 3 beats measurements. All measurements were performed by two experienced electrophysiologists. Response to CRT was defined as at least 20 milliseconds decrease in the QRS duration in lead V3 at 6-months follow-up. Random measurements of some unnamed ECGs and EGM delays

repeated and the agreement between measurements was greater than 90%.

Statistical analysis

SPSS version 18 software was used for data entry and analysis. Mean ± SD of quantitative data and frequency of qualitative data were calculated and reported. Differences between quantitative data before and after any stage of pacing were analyzed by paired sample T-test. Chi square test was used to estimate differences between qualitative data. Parametric and non-parametric bivariate correlations between continuous variables were calculated and corresponding graphs were plotted. P value < 0.05 was considered as statistically significant.

Results and Discussion

Fifty-seven patients fulfilled the inclusion criteria and were enrolled. However, six patients expired during 6-months follow-up. Fifty-one patients attended the 6-month follow-up visit and were included in data analysis. Study population consisted of 36 men and 15 women with mean age 60± 14 and 57 ± 18 years; respectively. All variables had normal distribution except for the LV50 QRS duration. Electrical response to CRT defined as narrowing of ≥20 msec in QRS width after simultaneous Biv pacing (simul QRS) (Frederic A. Sebag *et al.*, 2012). By this definition 40 (78.4%) patients (27 men and 13 women) were responder. Majority of patients had ischemic cardiomyopathy (90.2%) and dominant bundle branch block was LBBB (86.3%). Baseline characteristics are shown in table 1. Mean intrinsic QRS duration (IQRS) was 166.84 ± 22 msec which decreased to 140.43 ± 23 msec after simultaneous Biv pacing (P<0.0001). Mean QRS reduction was 26.60 ± 29 msec.QRS narrowing index [(intrinsic QRS – simul QRS) / intrinsic QRS duration)*100] (John Rickard *et al.*, 2011) in all, responder and non-responder patients were 14.9%, 24.46% and -3.83 respectively (P <0.001).

Mean intrinsic EGM delay was 67 ± 36 msec for all patients. This delay was72± 33 in patients with LBBB and 11.25 ± 13 in other patients (P= 0.001). The intrinsic EGM delay between patients with and without electrical response to CRT was not significant (69.96 ± 36 and 52.75 ± 37, P = 0.2). Correlation between Simul QRS and intrinsic EGM delay was not significant in all patients (correlation coefficient (cc) = 0.30, P= 0.07), but in subgroup of patients with LBBB this correlation was significant (Figure 1). In patients with LBBB correlation between simul QRS duration and RV only pacing EGM delay (cc = 0.28, P = 0.09) and LV50 (cc = 0.02, P = 0.89) was not significant.

Delta QRS defined as difference between IQRS and Simul QRS (John Rickard *et al.*, 2011). Mean delta QRS in all patients, electrical responders and not-responders were 26.6 ± 29, 42.75 ± 15 and -3.53 ± 23 respectively (P < 0.001).

Correlations between simultaneous QRS duration and QRS duration of other forms of CRT pacing are shown in Table 2.There was significant correlation between Simul QRS and RV only QRS (Figure 2), and also with LV50 pacing QRSin all patients and subgroups of patients (patients with LBBB and responder ones). Correlation between simul QRS duration and intrinsic QRS duration in all patients was not significant, but among patients with electrical response there was a weak correlation.

The primary goal of this study was to evaluate the effects of intrinsic EGM delay between RV and LV leads on simul QRS duration. Mean QRS width reduction was 26.60 ± 29.80 (a little skewed distribution) and 78.4% of patients were electrically responder. QRS narrowing index in all, responder and non-responder patients were 12.5% and 24.46% and -3.8% respectively. The findings of the present study are in accordance with previous reports in terms of percent of electrical response and narrowing of QRS (John Rickard *et al.*, 2011; Coppola, 2016; Coppola and Corrado, 2014).

Despite the significant difference between intrinsic EGM delay in patients with and without LBBB, there was no difference between responders and non- responders. Marta de Riva-Silva *et al*. in their study report EGM delay of 93 msec in responders and 69 msec in non-responders (John Rickard *et al.*, 2011). Tina Lin *et al.*, (2014) and Michael R. Gold *et al.*, (2016) also reported similar results in their reports. Annamaria Kosztin *et al.*, (2015) in their manuscript confirmed the importance of EGM delay and its predictive value in clinical outcome of patients (Annamaria Kosztin and Vivien Klaudia Nagy, 2015). The method of measuring EGM delays in the present study was similar to those reports. However, the mean EGM delay in our study (66.9msec) was in the range of non-Responder groups of those studies. Along with our results Marcus Mutschel knauss *et al*. didn't report any significant correlation between VV delay and QRS narrowing. This discrepancy in our results might be due to the time of study. Additionally, intraoperative

measurements were reported in previous reports in contrast to data at 6-months follow-up in the present study. Some degrees of electrical remodeling and decrease in EGM delay is expected in this time period (Antonio D'Onofrio and Antonio De Simone, 2016).

Simul QRS duration showed a significant correlation with RV only and LV50 pacing QRS durations but no correlation with intrinsic QRS duration. Although the focus of most studies was on EGM delays but what is important is the QRS duration and QRS morphology, which is not completely related to EGM delay.

Table.1 Baseline characteristics of patients based on electrical response to CRT-D

	Responder 40 (78.4)	Non Responder 11 (21.6)	Total	P value
Male	27 (75)	9 (25)	36 (70.6)	0.3
Age (y)	57.2 ± 19	59.3 ± 18	57.8 ± 16	0.9
ICMP	35 (76.1)	11 (23.9)	46 (90.2)	0.3
LBBB	34 (77.3)	10 (27.7)	44 (86.3)	0.52
RBBB/IVCD	6 (85.7)	1 (14.3)	7 (13.7)	
Sinus	38 (79.2)	10 (20.8)	38 (94.1)	0.5
HLP	13 (81.3)	3 (18.8)	16 (31.4)	0.5
HTN	21 (84.4)	4 (16)	25 (49)	0.27
DM	17 (77.2)	5 (22.8)	22 (43.1)	0.45
Current SMK	11 (84.6)	2 (15.4)	13 (25.4)	0.52
MI	22 (78.6)	6 (21.4)	28 (54)	0.6
Lead Position	29 (78.4)	8 (21.4)	37 (72.5)	NS
Posterolateral	8 (88.9)	1 (11.1)	9 (17.6)	
Posterior Anterolateral	3 (60)	2 (40)	5 (9.8)	
Creatinine	1.16 ± 0.39	1.18 ± 0.51	1.16 ± 0.42	0.92
LVEF	28.0 ± 7	27.7 ± 4.1	27.9 ± 6.4	0.9
LVEDD	6.0 ± 1	5.7 ± 0.8	5.95 ± 0.9	0.34
Beta blocker	23 (85.2)	4 (14.8)	27 (52.9)	0.16
Diuretic	36 (76.6)	11 (23.4)	47 (92.1)	0.46
ACEI/ARB	32 (74.4)	11 (25.6)	43 (84.3)	0.14
QRS durations				
Intrinsic	173.82 ± 13	153.8 ± 29	166.84 ± 22	0.004
Simultaneous Biv	131.07 ± 16	157.33 ± 26	140.23 ± 23	<0.001
P value	<0.001	0.52	<0.001	

Fig.1 Correlation between simultaneous Biv pacing QRS and intrinsic LV to RV EGM delay in patients with LBBB

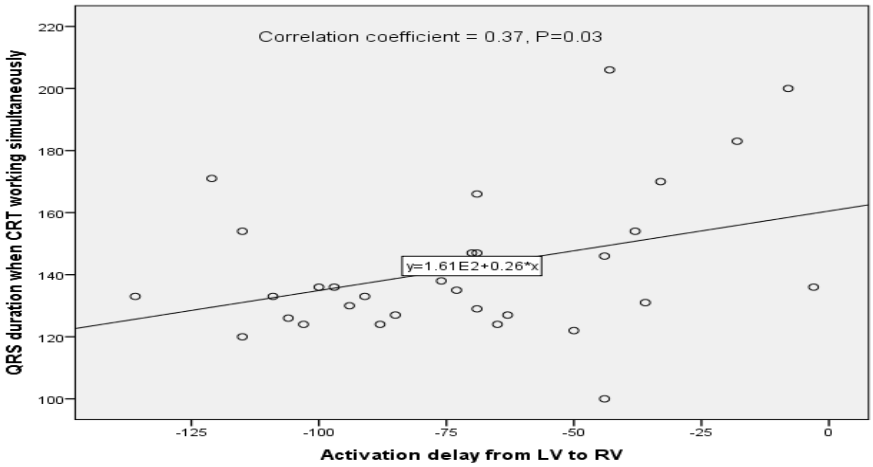
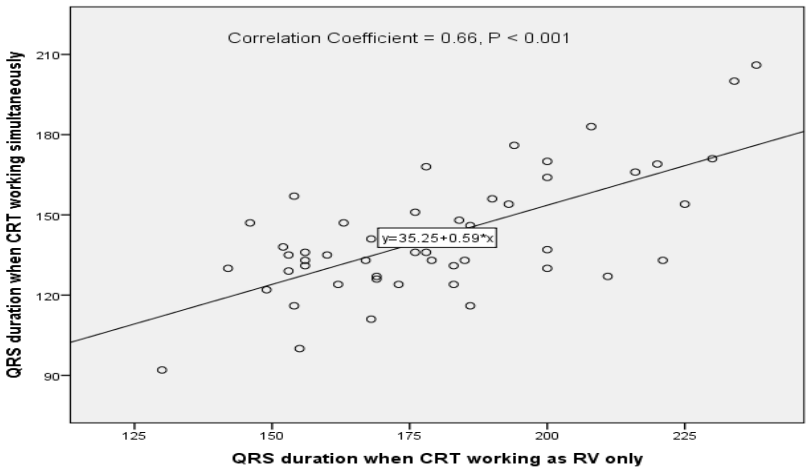


Fig.2 Correlation between simultaneous Biv pacing and RV only pacing QRS duration



ECG is a simple and readily available tool however it is not wildly used in the follow-up evaluation of patients with CRT therapy [23].Accordingly, we tried to incorporate findings of surface ECG and QRS duration[23]in this study in the follow-up evaluation of patients with implanted CRT. The findings of present study showed better correlation of simul QRS with RV only and LV50 pacing QRS, but not with intrinsic QRS duration. Although intrinsic QRS characteristics are important in selecting patients for implanting CRT device[1]it is not a robust predictor of response to therapy [24].This also pertains to the intrinsic EGM delay. What happens in the real world of CRT is pacing from RV and LV to obviate the interventricular dyssynchrony and the response is most probably achieved through narrowing of QRS[16,24]. Interactions between electrical forces and vectors from RV and LV compose QRS. Therefore ventricles affected by fibrosis and conduction disturbances may display dissimilar responses to pacing from RV and LV and form unpredictable QRS, which is not necessarily related solely to EGM delay. Based on these explanations it is reasonable to consider QRS characteristics in different pacing modes for better appreciation of response to CRT [23] Correspondingly Jeff M. Hsing *et al*. reported the influence of LV pacing QRS duration on response to CRT[24].

Conclusion

QRS narrowing showed no correlation with intrinsic EGM delay. There was strong correlation between simul QRS with RV only and LV50 paced QRS. We suggest measuring simul, RV only and LV50 paced QRS duration in operating room find best places for implanting RV and LV leads.

Limitations

This study is limited by relatively low number of patients. Additionally, majority of the implanted devices didn't have the capability of LV only pacing so we used LV50 pacing which may not be a true reflect of LV pacing. We did not evaluate hemodynamic response to CRT.

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Conflict Interest

The authors declare that there are not conflicts of interest.

References

Annamaria Kosztin VK, Vivien Klaudia Nagy. Longer right to left ventricular activation delay at cardiac resynchronization therapy implantation is associated with improved clinical outcome in left bundle branch block patients. Europace 2015, DOI: 10.1093/europace/euv117

Antonio D'Onofrio a AIb, Antonio De Simone. Electrical remodeling after cardiac resynchronization

therapy and its relationship with the anatomical remodeling. International Journal of Cardiology 2016;211:86-7.

Clyde W. Yancy, M., Mariell Jessup, Biykem Bozkurt. 2013 ACCF/AHA Guideline for the Management of Heart Failure, A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2013;128:e240-e327.

Francesco Zanon M, Enrico Baracca, Gianni Pastore. Determination of the Longest Intra-Patient Left Ventricular Electrical Delay May Predict Acute Hemodynamic Improvement in Cardiac Resynchronization Therapy Patients. Circulation, Arrhythmia and Electrophysiology 2014;7(3):377-83.

Frederic A. Sebag, Raphael P. Martins, Pascal Defaye. Reverse Electrical Remodeling by Cardiac Resynchronization Therapy:Prevalence and Clinical Impact. J Cardiovasc Electrophysiol 2012, DOI: 10.1111/j.1540-8167.2012.02376.x:1-9.

G. Coppola PB, E. Corrado. The QRS narrowing index for easy and early identification of responder to cardiac resynchronization therapy. International Journal of Cardiology 2014;170(3):440-1.

Giuseppe Coppola a GCa, Giuseppe Stabile. Magnitude of QRS duration reduction after biventricular pacing identifies responders to cardiac resynchronization therapy. International Journal of Cardiology 2016;221:450-5.

Hana Cho M, Andreas S. Barth, Gordon F. Tomaselli. Basic Science of Cardiac Resynchronization Therapy Molecular and Electrophysiological Mechanisms. Circ Arrhythm Electrophysiol 2012;5:594-603.

Jagmeet P. Singh M, Dali Fan, E. Kevin Heist. Left ventricular lead electrical delay predicts response to cardiac resynchronization therapy. Heart Rhythm 2006;2006(3):1285-92.

Jagmeet P. Singh, Helmut U. Klein, David T. Huang. Left Ventricular Lead Position and Clinical Outcome in the Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy (MADIT-CRT) Trial. Circulation 2011;123:1159-66.

Jeff M. Hsing KAS, Christophe Leclercq. Paced Left Ventricular QRS Width and ECG Parameters Predict Outcomes After Cardiac Resynchronization Therapy, PROSPECT-ECG Substudy. Circulation: Arrhythmia and Electrophysiology 2011;4:851-7.

John Rickard, Zoran Popovic, David Verhaert. The QRS Narrowing Index Predicts Reverse Left Ventricular Remodeling Following Cardiac Resynchronization Therapy. PACE 2011;34:604-11.

Marc Strik FR, Angelo Auricchio. Electrical and Mechanical Ventricular Activation During Left Bundle Branch Block and Resynchronization. J of Cardiovasc Trans Res 2012;5:117-26.

Marcus Mutschelkanaus TR, David Altman. intraoperative interventricular delay not predict response to cardiac resynchronization therapy (CRT). Department of Cardiology, Department of Basel Hospital, Switzerland.

Marta de Riva-Silva MaLp-G, Ricardo Salgado-Aranda. Value of Intraoperative Electrical Parameters Obtained During Implantation of Cardiac Resynchronization Therapy Devices for the Prediction of Reverse Remodeling. Scientific letters / Rev Esp Cardiol 2014;67(10):854-64.

Michael R. Gold M, Jagmeet P. Singh, Kenneth A. Ellenbogen, Interventricular electrical delay is predictive of response to cardiac resynchronization therapy. JACC: Clinical Electrophysiology, 2016, DOI: 10.1016/j.jacep.2016.02.018

Michael R. Gold UB-G, Jagmeet P. Singh. The relationship between ventricular electrical delay and left ventricular remodelling with cardiac resynchronization therapy. European Heart Journal 2011;32(20):2516-24.

Michele Brignole AA, Gonzalo Baron-Esquivias. 2013 ESCGuidelines on cardiac pacing and cardiac resynchronization therapy. European Heart Journal 2013;34:2281-329.

Mohamed Loutfi MN, Salah Eltahan, Aly Abo Elhoda. Predictors of response to cardiac resynchronization therapy in chronic heart failure patients. The Egyptian Heart Journal 2016;68:227-36.

Mohit K Turagam PVaAGK. Standardization of QRS Duration Measurement and LBBB Criteria in CRT Trials and Clinical Practice. Current Cardiology Reviews, 2013, 9, 20-23 2013;9:20-3.

Nina Hakacova M, Anna M.C. Robinson, Charles W. Olson, MS. The relationship between mitral papillary muscles positions and characteristics of the QRS complex. Journal of Electrocardiology 2008;41:487-90.

Panfilov KHWJTTaAV. Influence of diffuse fibrosis on

wave propagation in human ventricular tissue. Europace 2007;9:vi38-vi45.

S. Serge Barold BH. Usefulness of the 12-lead electrocardiogram in the follow-up of patients with cardiac resynchronization devices. Part I. Cardiology Journal 2011;18(5):476-86.

Tina Lin PC, Hariharan Sugumar. Implant Electrical Characteristics Predict Response to Cardiac Resynchronization Therapy. World Journal of Cardiovascular Diseases 2014;4:513-21.

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