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ORIGINAL ARTICLE

V–V delay interval optimization in CRT using echocardiography compared to QRS width in surface ECG

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Abstract *Introduction:* CRT had become a standard of treatment for patients with drug refractory heart failure. The presence of many cases of non-responders raises the need for device optimization echocardiography that is an established tool used to optimize CRT programming, but it is time-consuming. It was not yet defined whether a QRS width-based strategy may be a helpful tool for device programming.
Aim of study: The aim of this study is to compare the optimal interventricular delay interval (V–V interval) obtained by echo with that obtained by a simpler method using QRS width in surface ECG.
Methods and results: Twenty patients with implanted CRT were enrolled. All patients underwent echocardiographic optimization of the (A–V interval) after which five different V–V intervals (LV + 30, LV + 60, RV + 30, RV + 60, L + R0) were compared measuring Left Ventricular Outflow Tract Velocity Time Integral (LVOT VTI) as a surrogate for ejection fraction. A 12-lead ECG was recorded and QRS duration was measured in the lead with the greatest QRS width. The ECG optimized V–V interval was defined according to the narrowest achievable QRS interval among the 5 V–V intervals. The echocardiographic-optimized V–V interval was defined according to the highest LVOT VTI among the 5 V–V intervals. The echocardiographic-optimized V–V interval was left ventricle + 30 ms in 2 patients (10%), left ventricle + 60 ms in 8 pts (40%), simultaneous pacing in 8 pts (40%) and right ventricle + 30 ms in 2 pts (10%).
ECG method (using QRS width), had 85% coincidence with the echocardiographic method (using LVOT VTI) (κ = 0.906), (r = 0.81 P < 0.001).

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Conclusion: Significant correlation appeared to exist during optimization of CRT between VV programming based on the shortest QRS interval at 12-lead ECG pacing and that based on highest LVOT VTI by echocardiography. A combined ECG and echocardiographic approach could be a more convenient solution in performing V–V optimization.

1. Introduction

Cardiac resynchronization therapy (CRT) has emerged rapidly as a therapeutic option for patients with drug-refractory heart failure. After this therapy, most patients show improvement in heart failure symptoms, exercise capacity, and left ventricular (LV) systolic performance. Moreover, a decrease in rehospitalization for heart failure and improved long-term survival compared with optimal medical therapy has been demonstrated.[1–5]

1.1. Current selection criteria for patients eligible for CRT include

- Moderate to severe heart failure (New York Heart Association [NYHA] classes III–IV) despite optimal medical therapy.
- Systolic dysfunction (LV ejection fraction [LVEF] $<35\%$).
- Wide QRS complex (QRS duration >120 ms).[6,7]

Despite these selection criteria and although the clinical results of CRT are promising, analysis of individual responses has revealed that almost 30% of patients do not exhibit any symptomatic or hemodynamic improvement: the so-called 'non-responders'.[8–10] One of the reasons for this may be suboptimal programming of the device, which has particular considerations as compared to standard pacemakers.[11]

The recent generation of CRT devices allowed optimization of the V–V interval because of the availability of interventricular offset. In daily practice, echocardiographic assessment of cardiac output using the left ventricular outflow velocity time integral at different V–V intervals may be the preferred approach to assess optimal V–V settings. Adjustment of interventricular pacing intervals further improved cardiac performance compared with simultaneous biventricular pacing in a relevant subgroup of patients.[12]

Although echocardiography is the most widely used technique to optimize CRT, the process is time-consuming and, as yet, not well standardized. It was conceivable that an alternative method could be sought, which proved reliable, non-operator dependent, inexpensive, and suitable to become a built-in feature of a CRT device.[13–15]

A wide QRS has traditionally been used as a marker of patients with mechanical dyssynchrony. Although relatively good correlation between interventricular dyssynchrony and QRS duration has been reported, no significant correlation existed between intraventricular dyssynchrony and QRS width.[16]

The ECG-optimized V–V interval is therefore deemed to be related to the least interventricular dyssynchrony. According to published reports, the greatest QRS width was deemed to reflect interventricular mechanical dyssynchrony.[17]

We aimed in this work to correlate the optimal interventricular (V–V) pacing interval obtained by echo (highest LVOT VTI) with the optimal V–V interval obtained by a simpler method based on the surface ECG (Narrowest QRS width).

2. Patients

Over a period of one year from January 2009 to January 2010, we studied 20 patients with sequential activation capability biventricular pacing system. They included 17 males and 3 females.

Ten patients were studied at the Critical care Department, Cairo University from the period of January 2009 till August 2009, while the other 10 patients were studied at the pacemaker follow-up clinic at the Department of Cardiology, University of Brescia, Italy.

- The following patients were excluded from the study: those with recent ischemic episode or correctable coronary heart disease, frequent atrial and/or ventricular premature beats, suboptimal echocardiographic window with poor image quality, uncorrected valvular disease or dysfunctional prosthetic valve, severe primary pulmonary disease, and those with atrial fibrillation.

3. Methods

3.1. Echocardiography study

All patients were subjected to transthoracic echocardiographic examination using ATL.HDI 5000 colored echocardiographic machine using a 3.5 MHz transducer.

An apical 5 chamber view was obtained, color flow and pulsed wave (PW) Doppler was positioned in the LVOT with calculation of VTI. The left ventricular outflow tract (LVOT) velocity time integral (VTI) was measured at baseline and at five different V–V intervals (L + R 30, L + R 60, L + R 0, R + L 30, R + L 60).

The LVOT VTI is considered as a surrogate of stroke volume according to the following equation:

Flow rate = CSA (cross sectional area) × flow velocity.
SV (stroke volume) = CSA × VTI.
CO (cardiac output) = SV × HR.

The echocardiographic – optimized V–V interval is defined as that corresponding to the maximum LVOT flow velocity integral measured in cm (Fig. 1).

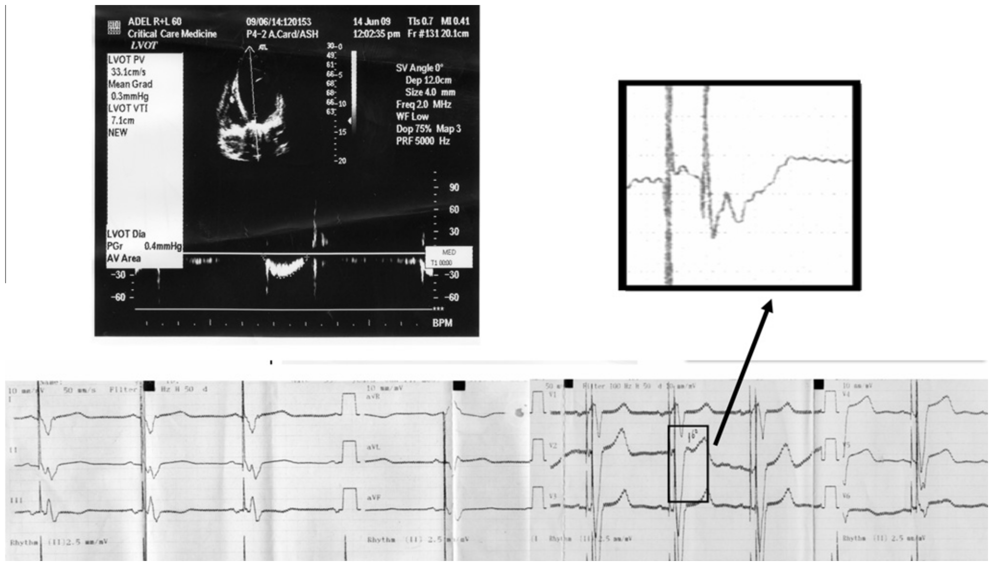

Figure 1 Simultaneous left and right ventricular pacing showing QRS width at lead V2 was 160 ms and aortic flow velocity was 7.1.

3.2. Electrocardiography measurements

At each of the five tested V–V intervals, a 12-lead electrocardiogram was recorded at a paper speed of 50 mm/s and a 10-mm/mV gain, and QRS duration in ms. was measured in the lead with the greatest QRS width from the first deflection of the QRS complex to its terminal isoelectric component (Fig. 1).

The electrocardiographic (ECG) – optimized V–V interval is defined as that corresponding to the narrowest QRS in these five measurements.

QRS duration was assessed manually using a graduated measuring instrument with accuracy of 0.25 mm (10 ms) in the lead with the widest QRS width at the 5 VV offsets.

4. Results

4.1. Baseline characteristics (Table 1)

Table 1 Population baseline characteristics, values expressed as mean ± SD, percent, or number (percent).

Age (yrs)	58.55 ± 14.04
Sex	
Males	85% (17)
Females	15% (3)
New York Heart Association class	
III	90% (18)
IV	10% (2)
Underlying cause of heart failure	
Ischemic	55% (11)
Non-ischemic	45% (9)
QRS width (ms)	169.5 ± 20.12
Left ventricular EF (%)	31.75 ± 5.53
Left ventricular end-diastolic diameter (cm)	6.88 ± 0.57
Left ventricular end-systolic diameter (cm)	5.67 ± 0.64
Risk factors	
DM	11 (55%)
HTN	11 (55%)
Smoking	10 (50%)
Duration of implant range in months	3.11 ± 2.86
Type of PM	
CRT-P	16 (80%)
CRT-D	4 (20%)

4.2. ECG optimized V–V interval

After performing an ECG with each of the five V–V delays, the ECG optimized V–V interval as defined by the narrowest QRS width was as follows.

Ten patients (50%) had the narrowest QRS with simultaneous biventricular pacing, 8 patients (40%) with left ventricular preactivation at 60 ms, and the remaining 2 patients (10%) with left preactivation at 30 ms (Table 2).

4.3. Echocardiographic results

The echocardiographic optimized V–V (defined as the highest LVOT VTI) at different settings of V–V interval programming was as follows.

Eight patients (40%) obtained the highest LVOT VTI reading with simultaneous biventricular pacing (L + R 0), 8 patients (40%) obtained it with left ventricular preactivation of 60 ms (L + R 60), 2 patients (10%) had their highest reading with left preactivation of 30 ms (L + R 30), the remaining 2 patients (10%) obtained the highest LVOT VTI with right ventricular preactivation of 30 ms (R + L 30) (Table 2).

4.4. Comparison between echocardiographic and electrocardiographic optimization of V–V interval

When comparing the echo and ECG optimized V–V interval, concordance between the two methods occurred in 17 patients (85%).

Table 2 ECG and echocardiography optimized V–V interval.

ECG optimized V–V interval	No. of patients	Percent	Echo optimized V–V interval	No. of patients	Percent (%)
L + R 0	10	50	L + R 0	8	40
L + R 60	8	40	L + R 60	8	40
L + R 30	2	10	L + R 30	2	10
R + L 30	0	0	R + L 30	2	10

Table 3 Cross tabulation between ECHO and ECG results.

V–V interval	L + R 0	L + R 30	L + R 60	R + L 30	Total
L + R 0	8	0	1	1	10
L + R 30	0	2	0	0	2
L + R 60	0	0	7	1	8
Total	8	2	8	2	20

The cross-tabulation between the 2 methods revealed Substantial concordance ($\kappa = 0.906$) between the ECHO optimized and ECG optimized V–V interval. P value < 0.001, Table 3.

4.5. Correlation between ECG and ECHO in determining the optimal V–V interval

There was high correlation between echo optimized V–V interval and ECG optimized V–V interval with $r = 0.756$ with P-value < 0.001 (Fig. 2).

4.6. ECG optimized V–V interval and Ischemic heart disease

Patients were divided according to the presence (Group I) or absence (Group II) of ischemic heart disease:

I – Group I (11 patients): 6 patients (54.5%) obtained the narrowest QRS width with left ventricular preactivation at 60 ms, 4 patients (36.4%) with simultaneous biventricular pacing and finally 1 patient (9%) with left ventricular preactivation at 30 ms.

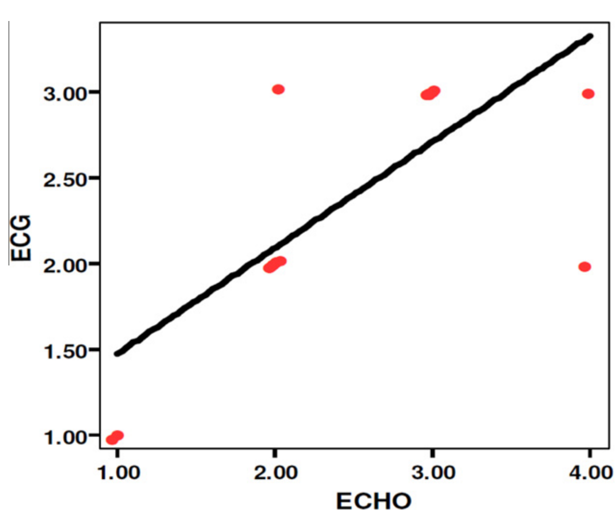

Figure 2 Correlation between ECG and ECHO.

II – Group II (9 patients): 6 patients (66.7%) had their narrowest QRS width with simultaneous biventricular pacing, 2 patients (22.2%) with left preactivation at 60 ms, and 1 patient (11.1%) with left preactivation at 30 ms (Table 4).

4.7. Echocardiographic optimized V–V interval and ischemic heart disease

I – Group I (11 patients): 6 patients (54.5%) obtained the highest LVOT VTI with left ventricular preactivation at 60 ms, 3 patients (27.3%) with simultaneous biventricular pacing, 1 patient (9.1%) with left ventricular preactivation at 30 ms, and finally 1 patient (9.1%) with right ventricular preactivation at 30 ms.

Group II (9 patients): 5 patients (55.6%) had their highest Aortic flow velocity with simultaneous biventricular pacing, 2 patients (22.2%) with left preactivation at 60 ms, and 1 patient (11.1%) with left preactivation at 30 ms, finally 1 patient (11.1%) obtained the highest reading with right ventricular preactivation of 30 ms (Table 5).

4.8. Concordance and ischemic heart disease

Group I (11 patients): 9 patients (81.8%) had concordance between the echocardiographic and ECG-optimized V–V interval, while in 2 patients (18.2%) there was no concordance observed.

Table 4 Relation between IHD and ECG optimized V–V interval.

V–V interval	Group I	Group II	P-value
L + R 0	4 (36.4%)	6 (66.7%)	0.329
L + R 30	1 (9.1%)	1 (11.1%)	
L + R 60	6 (54.5%)	2 (22.2%)	
Total	11	9	

Table 5 Effect of IHD on ECG optimized V–V interval.

V–V interval	Group I	Group II	*P*-value
L + R 0	3 (27.3%)	5 (55.6%)	0.508
L + R 30	1 (9.1%)	1 (11.1%)	
L + R 60	6 (54.5%)	2 (22.2%)	
R + L 30	1 (9.1%)	1 (11.1%)	
Total	11	9	

Table 6 Concordant patients and IHD.

Concordance	Group I	Group II	*P*-value
YES	9 (81.8%)	8 (88.9%)	1.0
NO	2 (18.2%)	1 (11.1%)	
Total	11	9	

Group II (9 patients): 8 patients (88.9%) had concordance between the echocardiographic and ECG-optimized V–V interval, while in 1 patient (11.1%) there was no concordance observed *P*-value = 1.000 (Table 6).

5. Discussion

In our study, we found that 17 patients (85%) had concordance between echo and ECG optimized V–V interval. A substantial agreement between these two methods used to optimize the V–V interval of CRT devices (weighted $\kappa = 0.906$, $P < 0.001$). Optimizing CRT devices with this ECG parameter showed a good correlation with the results obtained via echo-guided optimization of V–V interval ($r = 0.756$ with *P*-value < 0.001).

Our results are in agreement with the study conducted by Bertini et al.[18] who found a significant concordance during biventricular pacing between V–V programming based on the shortest QRS interval at 12-lead ECG pacing and echocardiographic-guided V–V interval optimization using LVOT VTI and recommended that a combined ECG- and echocardiographic approach could be a less time-consuming solution in performing this operation.

In contrast Vidal et al.,[19] reported a poor correlation between the V–V interval that produced the narrowest QRS interval (measured from the pacing artifact) and the V–V interval that obtained the best interventricular resynchronization according to tissue Doppler measurement.

The disagreement could be explained that Vidal et al.,[19] optimized the VV interval with a different method than that used in our study. Also, in our study we measured the QRS width from the first deflection, avoiding the initial isoelectric portion, While Vidal et al.[19] measured from the beginning of the pacing artifacts, in this latter ECG method there is an overestimation of QRS duration that may change at the different VV intervals tested, potentially affecting the final results.

At present, echocardiography is the most used technique to optimize CRT pacing, and the QRS duration is considered an oversimplified surrogate marker of mechanical dyssynchrony.[20] although most investigators use the velocity–time integral method, several echocardiographic measurements have been described for performing VV optimization. However, all require time and expertise.[20–22]

The maximal VTI by echo was found to be with LV preactivation in 50% (10 patients), 40% (8 patients) with simultaneous pacing (L + R = 0) and the remaining 2 patients with RV preactivation.

The optimum V–V interval involved in most patients was with LV preactivation in the studies conducted by Perego et al.[23] and van Gelder et al.[24] who obtained, respectively, 75% and 83% of LV preactivation as the optimal V–V interval in a similar group of patients with heart failure, systolic LV dysfunction, and LBBB configuration.

This is logical up to a certain point because all patients had a LBBB configuration, suggesting that the latest activation is located at the left lateral wall, and that pacing from the epicardium will have a delay of about 30–40 ms that should be corrected.

Burri et al.[25] investigated the role of sequential VV pacing in improving LVEF in 27 patients with heart failure using radionuclide ventriculography. Simultaneous biventricular pacing yielded maximal LVEF in only 33% of patients. A relative increase in LVEF of 18% by optimized sequential pacing was observed in the remaining patients. A significant impact on interventricular dyssynchrony but not intraventricular dyssynchrony by sequential VV pacing was observed in this study.

In normal hearts, the activation of the two ventricles does not occur simultaneously (i.e. epicardial RV depolarization starts a few milliseconds earlier than LV depolarization).[26] Second, in CRT, the left ventricle is paced from the epicardial side, and this could account for a delay in the transmission of the stimulus that needs to reach the subendocardial conduction system before spreading to the remaining ventricle.

Finally, the ventricular leads (particularly LV leads) are placed in quite different anatomical positions, depending on the operator's choice and coronary sinus anatomy, leading to ventricular activation patterns during pacing that differ from patient to patient.[27]

In our study population, there were 11 patients with underlying ischemic heart disease and 9 patients with no evidence of ischemia. Within the ischemic group, it was noted that there was a higher prevalence of LV preactivation as in 63% of patients (7 patients) had their optimal V–V delay with LV preactivation, while 27% (3 patients) had their optimal V–V interval with simultaneous pacing, only 1 patient had RV preactivation.

In non-ischemic group however 55.6% of patients had their optimal delay with simultaneous pacing 33% 3 patients with left preactivation, finally 1 patient (11.1%) obtained the highest reading with RV preactivation.

However, there was no statistically significant difference between ischemic and non ischemic groups as regards VV interval activation sequence the *P*-value was not significant (0.508).

Similarly Bertini et al.[18] and Vidal et al.[19] did not find a difference or prevalent mode between ischemic patients and non-ischemic patients.

Myocardial disease is associated with different locations and sizes of scars, and heterogeneity of conduction disturbances. The baseline ventricular conduction defect differs considerably from case to case, especially in patients with a QRS duration > 150 ms.

Theoretically, there is a slow conduction in the presence of scar tissue in ischemic cardiomyopathy and this necessitate more LV pre-excitation for further improvement of the overall response to CRT.[28]

Sogaard et al.[29] used Doppler imaging techniques, studied 21 patients with LBBB, QRS >130 ms, and New York Heart Association (NYHA) functional class III or IV heart failure, they defined a new parameter that they called the extent of delayed LV longitudinal contraction (DLC), this is calculated using tissue Doppler imaging (TDI) coupled with strain rate analysis.[29]

A segment was considered to have DLC if the strain rate analysis demonstrated motion reflecting true contraction and if the end of the segmental contraction occurred after aortic valve closure. DLC in patients with idiopathic dilated cardiomyopathy was identified in the lateral and posterior LV walls. In contrast, ischemic cardiomyopathy exhibited DLC more frequently in the septal and inferior walls.[29]

They concluded that the location of DLC predicted the optimal sequential CRT as posterior lateral wall DLC was associated with optimal sequential CRT via LV pre-activation, while septal and inferior wall-DLC was associated with optimal sequential CRT via RV preactivation.[29]

The practical interest of our study was the possibility of using a combined approach for VV interval optimization, of course, ECG cannot provide complementary information regarding LV dimensions, volumes, function, and synchrony in the way echocardiography does. However, our results show that ECG optimization using a simple measurement is possible and offers an easy way to estimate the optimum V–V interval. Furthermore, the measurements can be done immediately after device implantation, even in the operating room, thus obtaining a good correlation with echo in more than 80% of patients with LBBB configuration.

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