Clinical Research

Determination of the optimal atrioventricular and interventricular delays in cardiac resynchronization therapy

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Objective In order to provide the maximum benefit of cardiac resynchronization therapy (CRT), we tried to use an echocardiographic method to optimize the atrioventricular and interventricular delay. Methods The study included 6 patients who underwent implantation of biventricular pacemakers for drug-resistant heart failure. Two-dimensional echocardiography and tissue Doppler imaging were carried out before and after the pacemaker implantation. The optimal AV delay was defined as the AV delay resulting in maximum time-velocity integral (TVI) of transmural filling flow, the longest left ventricular filling time (LVFT) and the minimum mitral regurgitation (MR). The optimal VV delay was defined as the VV delay producing the maximum LV synchrony and the largest aortic TVI. Results CRT was successfully performed in all patients. After pacemaker implantation, an acute improvement in left ventricular ejection fraction (LVEF) was observed from 26.5% to 35%. Meanwhile, the QRS duration decreased from 170ms to 150ms. The optimal AV delay was programmed at 130, 120, 120, 150 and 110ms respectively with heart rate corrected, LVEF significantly lengthened and TVI of MR decreased (non-optimal vs optimal AV delay: LVFT: 469ms vs 525ms; TVI of MR: 16.43cm vs 13.06cm, P<0.05). The optimal VV delay was programmed at 4, 4, 8, 12 and 8ms with LV preactivation respectively. Programming the optimal VV delay increased the aortic TVI from 17.33cm to 21.42cm (P<0.05). In the septal and lateral wall, peak systolic velocities improved from 2.70cm/s to 3.02cm/s (P<0.05) and from 1.31cm/s to 2.50cm/s (P<0.05) respectively. The septal-to-lateral delay in peak velocity improved from 56.4ms to 13.3ms after CRT (P<0.01). Conclusions Optimization of AV and VV delays may further enhance the efficacy of CRT. However, there was interindividual variability of optimal values, warranting individual patient examination. (J Geriatr Cardiol 2005; 2(4):207-210)

Key Words cardiac resynchronization therapy; optimal atrioventricular delay; optimal interventricular delay; tissue Doppler imaging

Heart failure (HF) is a major and an increasing public health problem, with an almost “epidemic” increase in the number of patients. Despite recent advances in pharmacotherapy, the prognosis remains poor. As a rapidly emerging and novel approach to HF treatment, cardiac resynchronization therapy (CRT) has been shown to offer hemodynamic and clinical improvement as well as survival benefit to HF patients by reducing contractile dyssynchrony. However, 20% to 30% of those patients did not respond to CRT. The remaining atrioventricular, inter- and intra-ventricular dyssynchrony after CRT may be one of the reasons for this nonresponsiveness. New echocardiography (ECHO) techniques, and in particular tissue Doppler imaging (TDI) analysis, has been proved to be a helpful tool in evaluating cardiac dyssynchrony, as well as in assessing the degree of cardiac resynchronization after biventricular device implantation. In this study, we optimized the atrioventricular and interventricular delays (AV delay and VV delay) to provide the maximum benefit of CRT using echocardiographic method.

Patients and Methods

Study population
This prospective study included 6 patients who underwent implantation of biventricular pacemakers for drug-resistant heart failure of the New York Heart Association (NYHA) class III and had at least minimum functional mitral regurgitation (MR).

Pacemaker implantation
Three transvenous inserted pacing leads were connected to a three-chamber biventricular pacemaker (Medtronic InSync III 8042, Medtronic Inc.) with programmable VV delay. In addition to the right atrial and right ventricular leads, there
was a coronary sinus lead, which was advanced into the lateral or posterolateral cardiac vein through a coronary sinus tributary.

**ECHO protocol for the prediction of optimal AV and VV delays**

Two-dimensional ECHO and TDI were carried out on the day before and after pacemaker implantation with a commercially available system (vivid 7 GE-Vingmed, Milwaukee, Wisconsin). Different AV and VV delays were examined in each patient. To assure a constant intrinsic sinus rhythm during the study, the pacemaker was programmed for AV sequential pacing with pacing rate below the patient’s intrinsic sinus rate while ≥ 50bpm.

During the AV delay examination, the maximum AV delay at which full ventricular capture was still preserved was identified under the ECG control. This value, lowered by 10ms, was designated as the testing AV delay till the minimum 80ms. Every time the testing AV delay was changed, the pulsed Doppler echocardiography of transmitral flow was performed once again. The following parameters indexed to heart rate were measured: left ventricular filling time (LVFT, time between the onset of E wave and the end of A wave), time-velocity integral (TVI) of diastolic transmitral filling flow, the velocity and TVI of systolic MR. In our study, the optimal AV delay was defined as the AV delay resulting in maximum TVI of transmitral filling flow, the longest LVFT and the minimum MR.

During the VV delay evaluation, examinations were carried out at 7 different VV delay intervals with LV lead preactivation (4, 8, 12, 20, 40, 60, 80ms) and 2 different VV delay intervals with RV lead preactivation (4, 8ms). Thus, a total of 9 different VV delays were examined with an equilibrium period of 5 minutes between each examination. Two methods were used to determine the optimal VV delay. First was to place the sample volume in the basal portions of the septal and the lateral wall. Peak systolic velocities and time to peak systolic velocities were obtained, and the septal-to-lateral delay in peak velocity was calculated as an indicator of LV dyssynchrony. Second was to maximize the cardiac output (CO), which was determined as the largest aortic TVI using the Doppler technique. In our study, the optimal VV delay was defined as the VV delay that resulted in the maximum LV synchrony and the largest aortic TVI.

**Statistical analysis**

All data were expressed as mean ± SD. For the comparison of parametric variables at different AV or VV delays, paired sample t test was used. P<0.05 was considered statistically significant.

**Results**

Six patients were included in the study. The underlying etiology of heart failure was idiopathic dilated cardiomyopathy. All patients were in NYHA class III and had left bundle branch block with QRS duration ≥ 150ms. The mean LVEF was 26.

![Figure 1: Regional myocardial velocity curves obtained by tissue Doppler imaging at the basal septal (yellow) and basal lateral (green) segments. A: There was septal-to-lateral delay in peak velocity with low velocity, especially in the lateral wall. B: After CRT, systolic synchronicity was achieved, as reflected by the overlapping of velocity curves. Furthermore, there was a dramatic improvement in the peak velocity of the lateral wall.](image)

5%, and the mean left ventricular end-diastolic dimension (LVEDD) was 78.8mm. The clinical and echocardiographic parameters of the six patients are summarized in Table 1.

**Baseline versus simultaneous CRT**

CRT was successfully performed in all patients. After pacemaker implantation, all patients had an improvement in symptoms and exercise capacity. An acute improvement in LVEF was observed from a mean of 26.5% to 35%. Meanwhile, the QRS duration decreased from a mean of 170ms to 150ms. The final pacemaker parameters and the echocardiographic values are summarized in Table 2.

**AV delay optimization**

According to ECHO protocol, the optimal AV delay was programmed at 130, 120, 120, 120, 150 and 110ms respectively (mean value=125ms). With AV delay shortening or lengthening from its optimal value, the heart rate corrected LVFT was both significantly shortened and TVI of MR was increased (nonoptimal vs optimal AV delay: LVFT: 469ms vs 523ms; TVI of MR: 16.43cm vs 13.06cm, P<0.05). However, TVI of diastolic transmitral filling flow did not differ significantly at the nonoptimal and optimal AV delays (24.15cm vs 25.28cm, P>0.05).

**VV delay optimization**

For these six patients, the optimal VV delay was...
Table 1 The clinical and echocardiographic parameters

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Gender (F/M)</th>
<th>Etiology</th>
<th>NYHAFC</th>
<th>LVEF(%)</th>
<th>LVEDD (mm)</th>
<th>QRS duration (ms)</th>
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<tbody>
<tr>
<td>1</td>
<td>59</td>
<td>F</td>
<td>DCM LBBB IAVB</td>
<td>III</td>
<td>34</td>
<td>59</td>
<td>170</td>
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<tr>
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<td>74</td>
<td>M</td>
<td>DCM LBBB IAVB</td>
<td>III</td>
<td>32</td>
<td>84</td>
<td>160</td>
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<tr>
<td>3</td>
<td>69</td>
<td>M</td>
<td>DCM LBBB IAVB</td>
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<td>5</td>
<td>40</td>
<td>M</td>
<td>DCM LBBB IAVB</td>
<td>III</td>
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<td>6</td>
<td>70</td>
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<td>DCM LBBB IAVB</td>
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Table 2 Echocardiographic values before and after CRT and the optimal pacemaker parameters

<table>
<thead>
<tr>
<th>Case</th>
<th>QRS duration(ms)</th>
<th>LVEF</th>
<th>Optimal AV delay(ms)</th>
<th>Optimal VV delay(ms)</th>
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<tr>
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<td>Before CRT</td>
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Programmed at 4, 4, 8, 12 and 8ms with LV preactivation respectively. Programming the optimal VV delay increased the aortic TVI from 17.33cm up to 21.42cm (P<0.05). In the septal and lateral wall, peak systolic velocities improved from 2.70cm/s to 3.02cm/s (P>0.05) and from 1.31cm/s to 2.50cm/s (P<0.05), respectively. The septal-to-lateral delay in peak velocity improved from 56.4ms to 13.3ms after CRT (P<0.01).

Discussion

CRT is a new non-pharmacological approach for treatment of patients with moderate to severe congestive heart failure and inter- or intra-ventricular conduction delay and has been associated with improved NYHA functional class, increased exercise tolerance, better quality of life and survival benefit. In our study, after pacemaker implantation, an acute improvement in LVEF was observed from 26.5% to 35%. Meanwhile, the QRS duration decreased from 170ms to 150ms. The mechanisms underlying the therapeutic effect of CRT include improvement in the inter- and intraventricular contraction and relaxation synchrony and optimization of AV synchrony. However, previous studies showed that 20% to 30% of patients, even though selected according to traditional patients selection criteria (QRS>120ms, left bundle branch block, NYHA class III-IV and LVEF<35%), did not respond to CRT. This may be due, at least in part of these patients, to incomplete resynchronization—the remaining atrioventricular, inter- and intra-ventricular dyssynchrony. So, restoring physiologic AV timing and contraction synchrony is very important.

AV synchrony plays an important role in achieving maximum cardiac performance: with too long or too short an interval resulting in poor chamber filling and contributing to MR. In our study, the optimal AV delay was defined as the AV delay that provided the longest LVFT and the minimum MR. Although optimal AV delay value was set at 150ms, yet patients were still in P wave triggered biventricular pacing because most of them suffered from a first degree AV block.

Similar to that described by Meluzin et al, we found a relatively large interindividual variability of optimal AV delay ranging from 110ms to 150ms, warranting individual patient examination. Meanwhile, both lengthening and shortening the AV delay from its optimal value were associated with shortened LVFT and increased MR. The result was the same as a study done on patients with DDD pacemaker. In a recent study, Scharf C et al studied the optimal AV delay at various heart rates during CRT. Judging by the TVI of the left ventricular outflow tract, they found a positive linear relationship between an increase in heart rate, in optimal AV delay and in TVI. However, TVI of the left ventricular outflow tract, the "only" outcome parameter, may not precisely and fully reflect the impact of AV delay. Therefore, more studies on the optimal rate-dependent AV delay using other methods are needed.

Coordinate ventricular contraction depended on normal
ventricular activation. When a portion of the heart was prematurely stimulated, the activation sequence changed markedly, generating regions of both early and delayed contraction. The early contraction occurred when pressure was low and did not lead to ejection. The late contraction occurred at higher stress and resulted in paradoxical stretch of early contracting segments. The net result was a decline in systolic performance and a delayed relaxation. So, to maintain synchronicity of contraction was important. With the introduction of the InSync III device, it is now possible to optimize resynchronization with programmable VV delay.

A recent study indicated that hemodynamic effect could be reached by a moderate programmed VV delay of less than 20ms. It was also found that the optimal delay did not change significantly between before discharge from the hospital and 3 months later during the follow-up. In agreement with that study, our findings also showed that VV delay optimization resulted in a substantial reduction in septal-to-lateral delay and increase in aortic TVI, indicating resynchronization after CRT. Longer or shorter VV delay may even have a negative hemodynamic effect; therefore, VV delay should be guided by ECHO to optimize cardiac hemodynamics (Figure 1). In addition, LV synchrony and aortic TVI were found to be optimal within a very small range of VV delay (from 4ms to 12ms). Therefore, the native VV delay (4ms with LV preactivation) would be the best choice if ECHO for VV delay optimization was unavailable.

Conclusion

Cardiac resynchronization therapy was considered effective, with good clinical results, for patients with severe heart failure, although 20% to 30% of the patients did not respond to CRT. The programmable AV and VV delays had potent influences on the benefit of CRT. Modulation of AV and VV delays could optimize contractile synchrony, enhance the contribution of atrial systole, and reduce mitral regurgitation. However, there were interindividual variabilities of optimal values, warranting individual patient examination. So, it is necessary to optimize the pacemaker parameters, particularly AV and VV delays, in patients received CRT therapy.

References