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Doppler Echocardiographic Methods for Optimization of the Atrioventricular Delay during Cardiac Resynchronization Therapy

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Abstract

Cardiac resynchronization therapy (CRT) is beneficial for a majority of patients with medically-refractory heart failure due to severe left ventricular (LV) systolic dysfunction and prolonged interventricular conduction to improve symptoms and LV performance. An optimally programmed atrioventricular delay (AVD) during CRT can be also important to maximize the response in left ventricular function. Several Doppler-echocardiographic methods have been reported to be useful for determination of the optimal AVD. This review will discuss the various Doppler-based approaches to program the AVD in patients that receive CRT.

Keywords

Doppler Echocardiography; Heart Failure; Cardiac Pacing

Introduction

The response in left ventricular (LV) systolic performance in patients that receive cardiac resynchronization therapy (CRT) can be influenced by the programmed atrioventricular delay (1–3). There are several Doppler-echocardiographic methods to determine the optimal atrioventricular delay (AVD) that include pulsed-wave Doppler (PWD) measurements of mitral inflow velocities, continuous wave Doppler of the mitral regurgitant jet velocity envelope, or the systolic velocity time integral (VTI) by pulsed-wave Doppler in the LV outflow tract or continuous wave Doppler (CWD) recordings of peak aortic flow velocities. This review will discuss the various Doppler-echocardiographic methods that have been reported to program the AVD in patients that receive CRT.

Mitral inflow methods

Doppler-derived mitral inflow velocities for optimization of the AVD were initially reported in patients with complete heart block that received a dual-chamber AV sequential pacing device (4,5). The “Ritter method” was based on programming an AVD to eliminate prolonged AV conduction (i.e., PR interval) and to synchronize the end of late diastolic transmitral inflow (i.e., A-wave) with the onset of left ventricular contraction and maximize diastolic filling. The programmed AVD that maximally improved LV filling correlated with the improvement in peak endocardial acceleration determined by a sensing device in the

apically-positioned RV lead to measure global contractile function (4). A subsequent study reported AVD optimization by the Ritter method improved stroke volume, determined by impedance cardiography, compared to a fixed AVD interval (5). These investigators also noted that the Ritter method may not be applicable in patients with heart failure or restrictive LV filling and it was not reported in either investigation whether patients had impaired LV systolic function. Regardless, the Ritter method has been used for programming the AVD for CRT in clinical trials and in numerous single-center studies.

The Ritter method is a simple approach that requires measurements of the time from the ventricular paced deflection to closure of the mitral valve at a long AVD interval (i.e., 160–200 ms) and at a short AVD interval (i.e., 50–60 ms). It is important that the patient is 100% LV paced at the long AVD. The optimal AVD is determined as the difference between the two time intervals subtracted from the programmed “long” AVD interval (figure 1 and figure 2). At a long programmed AVD, the duration of late mitral inflow (i.e., A-wave) is preserved but at a short AVD the mitral A-wave duration decreases and may become “truncated”. However, a relatively short programmed AVD will maximally increase left ventricular diastolic filling time.

Another approach to program the optimal AVD is based on separation of the peak mitral E and A wave velocities or the “iterative method” to maximize LV diastolic filling. The CRT device is programmed at various AVD that will separate the LV inflow components (i.e., E-wave and A-wave) to improve LV diastolic filling. The effect of various programmed AVD in a patient with “fusion” of the E- and A-wave velocities prior to CRT are shown in figure 3. The “iterative method” represents another relatively simple approach to program the optimal AVD in CRT patients. This method however is subjective, nor has been compared to the response in stroke volume (i.e., aortic VTI) or invasive measurements. Furthermore, mitral inflow methods may be limited if the heart rate is increased, volume loading conditions, and have not been extensively evaluated during atrial pacing.

A retrospective study of 215 patients, initially programmed at an AVD between 100 – 120 ms at CRT device implant, were re-evaluated (mean 2 ± 4 days) for optimization of the AVD by mitral inflow methods (i.e., Ritter or iterative) (6). Figure 4 illustrates the various LV filling patterns that were reported in this investigation. The aim of the study was to program the AVD to achieve a LV filling pattern of impaired relaxation (IR) determined as a mitral E/A ratio < 1 . In this study, a subset of patients (49%) presented with IR at the time of echocardiography and re-programming the AVD did not significantly alter the LV filling pattern. However, in the patients with pseudonormalized or restrictive filling (i.e., mitral E/A > 1 , or > 2 , respectively), re-optimization of the AVD improved LV diastolic filling, based on a decrease by one grade, in 9%. Multivariate analysis disclosed AV sequential pacing, AV block, left atrial size, and LV ejection fraction were predictive of an optimal AVD > 140 ms. At follow-up after CRT (mean 13 months), there were no differences in the improvement of NYHA class, or mortality based on a final programmed AVD $\leq$ or > 140 ms. The authors proposed that in patients with a IR pattern of mitral inflow that receive CRT do not require Doppler optimization and the programmed AVD at device implant is likely optimal.

Another study evaluated measurements of the mitral inflow VTI during CRT at various programmed AVD (see figure 5) compared to invasive measurements of the rate of pressure development (7). The investigators reported that there were better correlations between mitral VTI and the increase in the invasive-determined peak (+) LV dP/dt, compared to the Ritter or aortic VTI methods (7). In this study, invasive measurements of stroke volume or cardiac output were not reported. In addition, the Doppler methods to determine aortic VTI used pulsed-wave Doppler recordings in the LVOT in half of the patients and CW Doppler

in the remaining group and it was not reported whether the presence of mitral regurgitation may have affected the results.

Another study described a “simplified approach” to program the optimal AVD during CRT by measurements of the time from termination of the mitral A-wave to the onset of the mitral regurgitation (MR) determined by pulsed-wave Doppler at 3 different programmed AVD that included invasive measurements of cardiac output (8). The programmed AVD that shortened the time from mitral valve closure to the onset of MR, (i.e., when developed LV pressure exceeds left atrial pressure) resulted in maximal improvement of cardiac output. However, patients in this study had received CRT for at least 3 months and were atrial-paced at 10 beats above their intrinsic heart rate. Thus, Doppler measurements were not reported during no CRT, or during intrinsic sinus rhythm.

The response in (+) LV dP/dt, determined by CW Doppler measurements of the time of acceleration in the mitral regurgitant jet velocity, to program the optimal AVD has been evaluated in one study (9). This method (see figure 6) represents an approach to program the optimal AVD based on invasive methods (2,3). The results demonstrated that optimization of the AVD by the Doppler-determined (+) LV dP/dt was superior to a fixed AVD of 120 ms, defined by the response in LV ejection fraction at 6 month follow-up. This method however requires the presence of a well-defined jet envelope by CW Doppler and an additional limitation, mentioned in this study, was the cycle-to-cycle variability in measurements of the Doppler-derived dP/dt was $\geq 40\%$.

Aortic outflow methods

The aortic outflow methods to program the optimal AVD are based on measurements of the systolic VTI that are determined by either pulsed-wave Doppler in the LV outflow tract or by continuous-wave (CW) Doppler at the aortic valve as an estimation of stroke volume (figure 7). Studies from our laboratory have relied on the CW Doppler-determined aortic VTI and measured during intrinsic conduction (prior to CRT) and at subsequent programmed AVD intervals (i.e., atrial synchronous ventricular pacing) at a long AVD of 200 ms and at each 20 ms decrement to a programmed AVD of 60 ms (10–13). At each programmed AVD, after 10 cardiac cycles of BIV pacing, the aortic VTI is measured in 3–5 consecutive beats and averaged. The optimal AVD was determined as the maximal increase in the aortic VTI compared to baseline. The advantage of CW Doppler-determined aortic VTI versus pulsed-wave Doppler measurements in the LV outflow tract are: 1) the pulsed-wave Doppler sample volume is fixed in location and can be influenced by cardiac motion during systole, 2) CW Doppler provides better demonstration of spatial flow characteristics due to the greater Doppler beam width, and 3) CW provides better definition of the spectral flow envelope with less cycle-to-cycle variability. Pulsed-wave Doppler-derived velocities in the LV outflow tract are necessary however, for programming the AVD in CRT patients with aortic stenosis.

Technical considerations regarding the use the aortic VTI method can include the time to perform the protocol at the various programmed AVD (including measurements) that require at least 15 minutes. Second, the echocardiographer must maintain a stable 2D image and the Doppler cursor position when obtaining Doppler velocities at each of the various programmed AVD. Third, measurements of the aortic VTI, due to cycle to cycle variability, should be averaged in at least 3 cardiac cycles. In situations where the average aortic VTI measurements at two programmed AVD are similar, the highest peak aortic velocity can be used to determine the optimal AVD.

In a randomized study of CRT patients (n = 40), the programmed AVD by the aortic VTI method resulted in better functional response, defined by NYHA class, and increases in

LVEF at 3 month follow-up compared to a group programmed at a fixed AVD of 120 ms (10). The optimal AVD that increased the aortic VTI was longer compared to the Ritter method in most patients that maximally increase LV stroke volume and there was no correlation between methods (11). However, LV diastolic filling time increased significantly regardless of the Ritter or the aortic VTI method and the optimal AVD. A preliminary study of various programmed AV delays during CRT on mitral inflow indices and the aortic VTI appears to be influenced by the pre-CRT mitral inflow LV diastolic filling pattern (12). In a follow-up study of 40 patients prior to and after 10 minutes of CRT, programmed at an optimal AVD determined by the aortic VTI method, the improvements in systolic function in the IR group were similar to the PNF/RF group (13). However, measurements of LV diastolic filling improved and LV filling pressures decreased only in the PNF/RF group, also reported in another study (6).

Programming the optimal AV delay: Mitral inflow versus aortic VTI methods

The differences between use of mitral inflow or aortic VTI methods to program the optimal AVD are likely due to several mechanisms. First, timing of mitral valve closure to the onset of isovolumic LV contraction to maximize improvement in the rate of left ventricular pressure development (peak + dP/dt) may have a variable effect on stroke volume in patients with severe heart failure (14). This likely reflects that stroke volume is measured during LV ejection after LV pressure has sufficiently developed and opening of the aortic valve. Second, patients with heart failure and increased LV volumes may require relatively elevated left ventricular end-diastolic pressures and an AV delay that decreases LV end-diastolic pressure may potentially decrease stroke volume (1). Third, the hemodynamic benefits of CRT are reported to be independent of changes in LVEDP (3). Fourth, the primary effect of CRT is to improve LV synchrony and systolic performance while the effects on LV diastolic function are often minimal (1). Therefore, a direct measurement of left ventricular systolic performance (i.e., stroke volume by aortic outflow VTI) may best determine the optimal AVD during CRT. A recent study compared the response in invasive measurements of peak (+) LV dP/dt at several AVD with Doppler measurements and reported the Ritter method was inferior to the aortic VTI method to program the optimal AVD (15). An example of the effects of the programmed AV delay on mitral inflow and aortic VTI at similar programmed AVD is illustrated in figure 8.

Determination of the optimal AVD with atrial pacing or during daily activity

Doppler methods for programming the optimal AVD in CRT patients that require atrial pacing or atrioventricular sequential pacing during CRT have not been extensively evaluated. In one study, measurements of the LV diastolic filling time, aortic TVI, and tissue Doppler indices of inter- and intraventricular synchrony were obtained during atrial-sensed biventricular pacing and during atrial pacing at 10 beats > intrinsic heart rate at a AVD of 40 ms greater than the AVD during atrial-sensed BIV pacing (16). During atrial pacing, the aortic VTI and LV diastolic filling time decreased, even after adjustment for changes in heart rate, and there was worsening of LV systolic and diastolic function. An example of the differences in the aortic VTI during intrinsic rhythm and atrial pacing at various AVD are illustrated in figure 9. Another study reported that during atrial pacing at a programmed AVD > 70 ms than the intrinsic-determined optimal AVD resulted in maximal improvement in the invasive-determined (+) LV dP/dt (15). The mitral inflow method was inferior to the CW Doppler-derived aortic VTI for programming the optimal AVD during atrial pacing.

Another study evaluated Doppler measurements of the aortic TVI to determine the optimal AVD in CRT patients during atrial pacing or immediately after exercise testing, at modest increases in heart rate (i.e., 20 beats per minute), compared to measurements obtained at rest

in the supine or seated position, respectively (17). Aortic TVI decreased with increases in heart rate during atrial pacing, and immediately post-exercise in the study patients. The investigators noted that longer AV delays were necessary for improvement in aortic VTI at increases in heart rate. These results were in contrast to when CRT devices are programmed in the rate-adaptive or “dynamic” mode that shortens the AVD with increased heart rate that occurs with physical activity.

These studies illustrate several salient findings: 1) atrial pacing is associated with reductions in stroke volume compared to intrinsic AV conduction, 2) the optimal programmed AVD is typically longer in CRT patients that require atrial pacing, 3) mitral inflow methods do not appear to be advantageous versus measurements of the aortic outflow VTI to program the AVD during atrial pacing, and 4) rate-adaptive or dynamic programming of the pacemaker device during activity may not be beneficial in CRT patients with regards to the effect on stroke volume. Further investigations are necessary with regards to the optimal programmed AVD in CRT patients due to variations in heart rate that occur with daily activity and in patients that require AV sequential pacing since echo-Doppler methods are universally performed in the supine position.

Additional considerations for programming the AVD during CRT

It has been reported the optimal AVD can change in patients that receive a CRT device during follow-up based on echo-Doppler measurements (10,18–20). The optimal AVD can either decrease or increase although the variations are often small (i.e., ~ 20 ms). One study evaluated a small series of CRT patients (n = 12) to determine whether measurements of systolic blood pressure by finger arterial plethysmography were related to changes in stroke volume by the Doppler aortic VTI method at various sensed and atrial-paced AVD at baseline and at 3 month follow-up (21). This approach is based on the increase in systolic blood pressure represents improved systolic performance in patients that received CRT as reported in invasive studies (2). Recently, some CRT devices now have intrinsic algorithms that may be used to determine the optimal AVD and obviate the need for Doppler-based methods at implant and during follow-up (15,22).

Conclusions

Doppler echocardiographic methods to program the AVD during CRT such as mitral inflow measurements are based on optimizing preload to increase stroke volume by the Frank-Starling mechanism. However, the presence of residual LV dilatation or impaired LV systolic function and the LV end-diastolic pressures are important considerations to determine the benefits of maximizing preload. The aortic outflow methods directly measure the relative changes in stroke volume but are relatively time-consuming and require the average of measurements at various AVD for programming the CRT device.

It is not established whether optimizing the AVD by Doppler echocardiographic methods, versus a “fixed” AVD (i.e., 100–120 ms) has long-term functional or clinical implications since no randomized trials have been conducted, nor if re-optimization of the AVD in patients that are “non-responders” to CRT are of benefit with regards to functional response or clinical outcomes.

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Figure 1.

Measurements of the time from pacing inflection to mitral valve closure at a short AV delay of 60 ms (left panel) and at a long AV delay of 160 ms (right panel). Note that the patient has a heart rate of 100 beats per minute and a mitral inflow pattern of pseudonormalized left ventricular filling. The optimal AV delay by the Ritter method was 80 ms and separated the mitral early (E) and late filling (A) velocities.

Figure 2. Measurements of the time from pacing inflection to mitral valve closure at a short AV delay of 60 ms (left panel) and at a long AV delay of 160 ms (right panel) in a patient with restrictive left ventricular filling. The optimal AV delay by the Ritter method was 70 ms. Note the mitral inflow pattern is similar at both programmed AV delays except for a increase in diastolic filling time at the AVD of 60 ms.

Figure 3.

Example of the iterative method to program the AV delay. Prior to CRT (top panel) there is fusion of the early (E) and atrial filling (A) velocities. The lower panels demonstrate the effect of various AV delays to separate E and A velocities. Note that at shorter AV delays there is maximal separation the E and A waves.

Figure 4. Mitral inflow patterns of impaired relaxation (E/A: 0.7, deceleration time or DT: 240 ms, panel A), pseudonormalized filling (E/A: 1.5, DT: 160 ms, panel B), and restrictive filling (E/A: 3.3, DT: 160 ms, panel C).

Figure 5. Measurements of the mitral velocity time integral (VTI) method to program the AV delay. Prior to CRT (top left panel) there is fusion of the early filling (E) and atrial filling (A) velocities and a mitral VTI of 21.5 cm. The subsequent panels demonstrate the effect of various programmed AV delays and measurements of the mitral VTI. Although shorter AV delays provided maximal separation the E and A waves, the maximal increase in mitral VTI was determined at a programmed AV delay of 140 ms.

Figure 6.

Example of the mitral regurgitant jet velocity envelope and measurements of the acceleration time to determine the (+) LV dP/dt prior to CRT (left panel) and at a programmed AV delay of 120 ms (right panel) during CRT. Note that diastolic mitral regurgitation (arrows) that was present prior to CRT was eliminated during CRT and the increase in the (+) LV dP/dt by 43%.

Figure 7. Measurements of the continuous-wave Doppler-derived aortic velocity time integral (VTI) to program the AV delay. Prior to CRT (top left panel) the aortic VTI was 31 cm. The subsequent panels demonstrate the effect of various programmed AV delays and the maximal increase (i.e., 36 cm) was determined at an AV delay of 140 ms. Note, this is the same patient illustrated in figure 3 and figure 5.

Figure 8. Measurements of the continuous-wave Doppler-derived aortic velocity time integral (top panels) and the mitral inflow velocity waveforms (bottom panels) at various programmed AV delays. The programmed AV delay of 180 ms maximally improved the aortic VTI but programmed AV delay of 120 and 140 ms better separates the mitral E- and A-wave velocities.

Figure 9.

Measurements of the pulsed-wave Doppler aortic outflow VTI during atrial-pacing (AP) at a heart rate of 70 bpm (left panels) and atrial-sensed (AS) biventricular (BIV) pacing at a heart rate of 58 bpm (right panels). Note the marked difference in TVI between AP and AS with BIV pacing off and during BIV at programmed AVD of 140 and 180 ms.