

AV Interval and Cardiac Output in Patients with Implanted DDD Pacemaker

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Abstract: Our aim was to compare the Cardiac Output (CO), Filling Time (FT) and Myocardial Performance Index (MPI) derived optimal atrioventricular delay (AVD) and to analyze systolic and diastolic performance at every optimal AVD. We studied 32 patients with implanted DDD pacemaker, from implantation time to 6 months following PM implantation, in Tabriz Shahid Madani Heart Center. The evaluation was performed during AV sequential pacing with different programmed AVDS ranged from 100-200 ms by steps of 20-30 ms. At every AVD, the following parameters were measured: FT, mitral VTI, ET, aortic VTI, ICT and IRT. CO and FT derived optimal AVDs were significantly different (146 ± 37 and 126 ± 35 ms, respectively), but their difference with MPI derived optimal AVDs was not significant (130 ± 28 ms). ICT/ET was similar at CO, FT and MPI derived optimal AVD (0.24 ± 0.10 , 0.22 ± 0.05 and 0.20 ± 0.07 , respectively). IRT/ET ratio was similar at CO, FT and MPI derived optimal AVDs (0.46 ± 0.14 , 0.45 ± 0.10 and 0.42 ± 0.10 , respectively).

Key words: Atrioventricular delay, cardiac output, DDD pacemaker

INTRODUCTION

Modern DDD (dual mode, dual chamber, dual sensing) pacemakers (PM) are complex, hugely capable devices incorporating new features that theoretically should enhance hemodynamics and therefore quality of life (Sulke *et al.*, 1992). In dual chamber pace makers, the interval corresponding to the intrinsic event, must be programmed. Optimization of this interval is critical in patients to obtain hemodynamic benefit from the pacemaker. Patients with dual chamber devices and prolonged native AV conduction are prone to develop episodes of output inhibition (Bode *et al.*, 1999). Programming of atrioventricular delay in patients with dual chamber pacemaker is very important for left ventricular filling and has a consequence for its stroke volume (Kubica *et al.*, 1993).

Pacemaker programming with the periodic echocardiographic evaluation of the optimal AVI, pacing rate and mode is imperative for optimal results (Topilski *et al.*, 2006). The efficacy of short Atrioventricular (AV) delay in patients with severe cardiac hypofunction has been reported (Ishikawa *et al.*, 2000). Cannon waves may be induced by programming excessively short AV intervals and diastolic mitral regurgitation may occur with excessively long programmed AV intervals. The AV interval is considered optimal (AV_{opt}) if it allows maximum cardiac output

(Melzer *et al.*, 2004). The duration of the optimal AV interval varies throughout a wide range among individuals, primarily the result of appreciable differences in interatrial conduction (Melzer *et al.*, 2004).

Atrioventricular Delay (AVD) is critical in patients with DDD pacemakers. Echo/Doppler evaluation of AVD providing the longest left ventricular Filling Time (FT) or the highest Cardiac Output (CO) is used for AVD optimization. Myocardial Performance Index (MPI) has been shown to improve by optimizing AVD (Porciani *et al.*, 2004). So, optimization of AVD significantly contributes to maximum cardiac performance (Melzer *et al.*, 2004; Meluzin *et al.*, 2004; Maurer *et al.*, 2003; Ishikawa *et al.*, 1999a). Improvement of cardiac function has been reported in patients with severely reduced cardiac function, by implanting DDD pacemaker and setting a short AV delay (Ishikawa *et al.*, 2000, 1999a).

Our aim was to compare the Cardiac Output (CO), Filling Time (FT) and myocardial performance index (MPI) derived optimal Atrioventricular Delay (AVD) and to analyze systolic and diastolic performance at every optimal AVD.

MATERIALS AND METHODS

The descriptive, cross sectional study was performed on patients underwent DDD pace maker implantation from 2004-2005 in Tabriz Shahid Madani Heart Center,

including the patients presenting for the day after analysis or the patients presenting for follow up during 6 months following PM implantation.

Thirty two patients (19 men and 13 women), aged 66 ± 17 years, mean ejection fraction 43%, with a DDD PM for sick sinus syndrome, CHB, or AV block Mobitz II, underwent echo/Doppler AVD optimization. Atrial leads were inserted in RV appendage and ventricular leads were implanted in RV apex. Concurrent with PM-analysis, Doppler and 2-Dimensional (2D) echocardiography was performed by commercially available instrument, VIVID-GE-Norway-7 echocardiograph. Indications for PM implantation and associated conditions were recorded for each patient. Patients with severe VHD and those with HR higher than pacing rate were excluded from the study.

Echocardiography in parasternal long axis view, for measuring LVOT (left ventricular outflow tract) diameter with optimal zooming, was performed on aortic valve. This diameter was used for calculation of LVOT cross section area as $2D \times 0.785$. Using four chamber apical view with sample volume at the apex of mitral valve leaflets, we measured mitral E/A, VTI and FT. Aortic ET and VTI was measured by 5 chamber view with sample volume at LVOT. IVRT was measured by four chamber apical view with sample volume within LVOT and mitral valve. The Heart Rate (HR) was 60-120 beat min^{-1} and we programmed the pacing rate at least 10 beats higher than patient own HR, to assure that HR is stable during the study. Calculating of LVOT and EF, we analyzed PM and programmed AVD at range of 100-200 ms by steps of 20-30 ms (100, 130, 150, 180 and 200 ms). At every AVD the following parameters were measured: FT, mitral VTI, ET, aortic VTI, ICT, IRT.

FT was calculated from beginning to end of mitral diastolic flow and followed with mitral VTI measurement. ET was calculated from beginning to end of aortic flow and followed with aortic VTI measurement. IVRT was calculated from end of aortic flow to beginning of mitral inflow. For calculation of IVCT, we used MCMO interval (the time between closing and opening of the mitral valve) and then $IVCT = MCMO - (IVRT + ET)$ formula. All parameters were calculated in 3 consecutive cycles. CO was calculated by $CO = SV \times HR$ formula ($SV = 2 \times D_{LVOT} \times 0.785 \times VTI_{LVOT}$). For calculation of MPI we used this formula: $MPI = ICT + IRT / ET$.

The collected data were analyzed by SPSS 12 statistical software. Values are expressed as mean \pm Standard Deviation (S.D.) unless indicated otherwise. The variables were compared by EP16 software using paired t-test and the $p < 0.05$ were considered significant.

RESULTS AND DISCUSSION

Of 32 studied patients 19 (59%) were male and 13 (41%) were female. The patients had the mean age of 66 ± 17 years (range of 14-84 year), mean LVEF of $43\% \pm 13$ (range of 15-66%) and mean HR of $84 \pm 12 \text{ beat min}^{-1}$ (range of 60-115). The mean LVEF in male and female patients was 41 and 46%, respectively. The indication of DDD implantation was SSS in 9 (28%), CHB in 20 (62%), AV block Mobitz II in 1 (3.1%) and HOCM (hypertrophic obstructive cardiomyopathy) in 1 (3.1%). Five patients had MI (3 antroseptal MI and 2 inferior MI). Mitral E/A in patients with DDD PM was < 1 in 24 (75%), $= 1$ in 5 (16%), > 1 in 2 (6%) and > 2 in 1 (3%).

Because of high HR and great difference of diastolic impairment in various AVDs, the assessment of mitral VTI and E/A in different AVDs was impossible.

CO and FT derived optimal AVDs were significantly different (146 ± 37 and 126 ± 35 ms, respectively) ($p = 0.01$), but their difference with MPI derived optimal AVDs was not significant (130 ± 28 ms) ($p = 0.09$). Optimal CO, MPI and FT derived ETs were 253 ± 41 , 257 ± 42 and 253 ± 41 , respectively, with no significant difference. Optimal CO and MPI derived IRTs were not significantly different (114 ± 28 and 108 ± 25 , respectively) ($p = 0.08$); also their difference with optimal FT derived optimal IRT was not significant (112 ± 22) ($p = 0.2$). Optimal CO and MPI derived ICTs were significantly different (59 ± 22 and 49 ± 15 , respectively) ($p = 0.01$), but their difference with optimal FT derived optimal ICT was not significant (53 ± 15) ($p = 0.2$).

ICT/ET was similar at CO, FT and MPI derived optimal AVD (0.24 ± 0.10 , 0.22 ± 0.05 and 0.20 ± 0.07 , respectively). IRT/ET ratio was similar at CO, FT and MPI derived optimal AVDs (0.46 ± 0.14 , 0.45 ± 0.10 and 0.42 ± 0.10 , respectively).

The patients were classified in 2 groups with $EF = 50$ and $EF < 50\%$. Then, the CO, MPI, FT, ICT/ET, IRT/ET and ET derived optimal AVDs were compared in 2 groups. The CO, MPI and FT derived optimal AVDs were not significantly different in 2 groups, but IRT/ET in optimal CO, MPI and FT were significantly different in 2 groups. Also, ET in CO derived optimal AVD was significantly different in 2 groups (Table 1).

Atrial contraction and AV synchrony is important in CO increase. In normal cases atrial contraction institute approximately 20% of ventricular filling, but this is more critical in LVH or ventricular diastolic impairment, higher ages and tachycardia (Møller *et al.*, 2000). Atrioventricular delay (AVD) is critical in patients with DDD pacemakers (PM), because it has good effect on atrial contractility, LV filling and stroke volume according the startling low (Porciani *et al.*, 2004).

Table 1: Comparison of optimal AVD in basis of various parameters in 2 group of EF<50 and EF ≥ 50%

EF/Optimal AVD	EF<50%	EF ≥ 50%	p-value
CO	151	133	0.2
MPI	133	121	0.2
FT	121	137	0.2
IRT/ET in basis of CO	0.49	0.37	0.2
IRT/ET in basis of MPI	0.45	0.35	0.01
IRT/ET in basis of FT	0.47	0.38	0.03
ICT/ET in basis of CO	0.25	0.19	0.08
ICT/ET in basis of MPI	0.2	0.17	0.3
ICT/ET in basis of FT	0.2	0.19	0.3
ET in basis of CO	243	275	0.04
ET in basis of MPI	250	273	0.1
ET in basis of FT	242	277	0.2
IRT in basis of CO	119	101	0.09
IRT in basis of MPI	113	93	0.04
IRT in basis of FT	114	104	0.2
ICT in basis of CO	61	51	0.2
ICT in basis of MPI	50	45	0.4
ICT in basis of FT	53	52	0.9

Optimization of programmed atrioventricular delay in dual chamber pacing is essential to the hemodynamic efficiency of the heart. Automatic AV delay optimization in an implanted pacemaker is highly desirable. Variations of Peak Endocardial Acceleration (PEA) with AV delay at rest correlate well with echocardiography derived observations, particularly with end-diastolic filling and mitral valve closure timings. This suggests the possibility of devising a procedure for the automatic determination of the Optimal AV Delay (OAVD) (Dupuis *et al.*, 2003). In patients with an implanted DDD pacemaker (PM), the atrial contribution may be interrupted by too short an atrioventricular (AV) delay and filling time may be shortened by too long an AV delay. The AV delay at which the end of the A wave on transmitral flow coincides with complete closure of the mitral valve may be optimal. Ishikawa *et al.* (1999b) concluded that optimal AV delay can be predicted by this simple formula: slightly prolonged AV delay minus the interval between end of A wave and complete closure of mitral valve at the AV delay setting. The QT interval on the surface ECG is strongly influenced by the atrioventricular (AV) delay setting and changes in the QT interval are closely related to changes in cardiac function. In patients with implanted DDD pacemaker, cardiac output is maximal when atrioventricular (AV) delay is set to give the maximum QT Interval (QTI). QTI is used as a sensor of a rate-responsive pacemaker and the evoked QTI (eQTI) is measured as the time duration from the ventricular pace-pulse and the T sense point, which is the steepest point of the intracardiac T wave (Ishikawa *et al.*, 2003). Changes in eQTI according to AV delay variation are greater in patients with reduced cardiac function than in those with normal cardiac function and the AV delay that gives the maximal eQTI can be easily determined in patients with reduced cardiac function. It has been

reported recently that implanting a DDD pacemaker and setting a short AV delay in patients with severely reduced cardiac function leads to improved function. The QT interval on the surface ECG is easily influenced by the AV delay setting and changes in the QT interval are closely related to changes in cardiac function (Ishikawa *et al.*, 2001, 2002). When CO was increased from the minimum to the maximum value by optimizing the AV delay, the QT interval was significantly prolonged. Cardiac output significantly increased when the QT interval was prolonged from the minimum to the maximum value by changing the AV delay. The QT interval changed according to the variations in AV delay and when the AV delay was set to give the maximum QT interval, CO was maximal (Ishikawa *et al.*, 2003).

Topilski *et al.* (2006) studied 28 patients with hypertrophic obstructive cardiomyopathy (HOCM). In this study, a protocol using echocardiographic examination assessing the changes in the Left Ventricular Outflow Tract (LVOT) gradient in different atrioventricular intervals (AVIs), pacing rates and pacing modes was used for optimal pacemaker programming. Twenty-five patients with HOCM were implanted with DDD pacemakers and evaluated prospectively. The LVOT gradient was measured during periodic evaluations every 3-6 months. After each evaluation, the optimal AVI, pacing rate and mode were set on the basis of the minimal LVOT gradient not associated with systolic arterial cuff pressure reduction. During follow-up, the optimal AVI was prolonged in most patients. Sixty-four percent of patients showed a clear relation between pacemaker modifications and gradient reduction. In 75% of these patients, optimal gradient reduction required repeated AVI and pacing rate programming on the basis of echocardiographic evaluation. The symptomatic reduction was positively correlated with the LVOT gradient reduction. In conclusion, DDD pacing is effective in reducing the LVOT gradient and improving functional capacity in adult patients with hypertrophic cardiomyopathy. Pacemaker programming with the periodic echocardiographic evaluation of the optimal AVI, pacing rate and mode is imperative for optimal results (Topilski *et al.*, 2006).

Kedia *et al.* (2006) evaluated the utility of atrioventricular (AV) optimization using Doppler echocardiography in patients who undergo Cardiac Resynchronization Therapy (CRT). Five hundred patients underwent CRT, 215 of whom underwent AV optimization <30 days after implantation. AV delay was optimized using Doppler mitral inflow data to target stage I diastolic filling. The mean follow-up period was 23 months. Baseline and final AV delay means were 120 +/-25 and 135 +/-40 ms, respectively. In 40% of patients (86 of 215),

final AV delay settings were >140 ms. There was no difference in mortality in patients with final AV delays of >140 ms. In this study, AV optimization in patients who underwent CRT resulted in final AV delay settings of >140 ms in 40% of patients. AV delay optimization based on Doppler echocardiographic determination of optimal diastolic filling is useful and safe in patients who undergo CRT (Kedia *et al.*, 2006).

Atrioventricular (AV) delay optimization can be an important determinant of the response to Cardiac Resynchronization Therapy (CRT) in patients with medically refractory heart failure and a ventricular conduction delay. In a study by Kerlan *et al.* (2006) 40 patients with severe heart failure, referred for CRT were studied using 2-dimensional Doppler echocardiography. In each patient, the acute improvement in stroke volume with CRT in response to 2 methods of AV delay optimization was compared. The optimized AV delay determined by the aortic VTI method resulted in an increase in aortic VTI of 19 +/-13% compared with an increase of 12 +/-12% by the mitral inflow method. The optimized AV delay by the aortic VTI method was significantly longer than the optimized AV delay calculated from the mitral inflow method (119 +/-34 ms and 95 +/-24 ms). So, AV delay optimization by Doppler echocardiography for patients with severe heart failure treated with a CRT device yields a greater systolic improvement when guided by the aortic VTI method compared with the mitral inflow method (Kerlan *et al.*, 2006).

There was a significant positive correlation between the optimal AV delay at which CO was maximal (161 +/-33 ms) and the optimal AV delay predicted from the maximum QT interval (167 +/-29 ms) (Ishikawa *et al.*, 1999a). Porciani *et al.* (2004) compared the CO, FT, MPI derived optimal AVD. Twenty-five patients with a DDD PM underwent echo/Doppler AVD optimization. CO, FT and MPI derived optimal AVDs were significantly different. ICT/ET was similar at CO, FT and MPI derived optimal AVD. IRT/ET ratio was similar at FT and MPI derived optimal AVDs and significantly shorter than at CO derived optimal AVD. Different methods indicate different optimal AVDs. However, analysis of systolic and diastolic performance shows that different AVDs result in similar systolic or diastolic performance. At MPI optimized AVD, a high CO combined with the most advantageous conditions of both isovolumic contraction and relaxation phases is achieved (Porciani *et al.*, 2004).

Porciani *et al.* (2006) studied 22 patients implanted with a biventricular device. The optimal AVD was

identified by the minimum MPI. After optimization, the appropriate AVD was programmed in each patient. MPI at 6-month follow-up after optimization was significantly higher compared with baseline. Re-optimization of AVD significantly reduced MPI compared with the value prior to re-optimization. The MPI remained unchanged at 12-month compared with 6-month follow-up. Clinical symptoms and reverse left ventricular remodeling were sustained at 6-month and 12-month follow-up. They concluded that optimal AVD changes over time in patients with heart failure. Sustained improvement in clinical symptoms and reverse left ventricular remodeling after CRT are not temporally associated with improvement in MPI (Porciani *et al.*, 2006).

Leonelli *et al.* (1997) designed a study to demonstrate the effects of varying the atrioventricular delay (AVD) on ventricular diastolic filling dynamics and the resultant stroke volume in patients with complete heart block and normal cardiac function. They studied 7 patients with normal cardiac function in whom a dual chamber pacemaker had been implanted because of complete heart block. Doppler and M-mode echocardiography was performed at 70, 100, 140, 180 and 220 ms, AVD with the device in DDD mode at a rate of 80 beats min⁻¹. Optimization of this interval, with a 19% increase in stroke volume was achieved in the group of patients at an AVD of 140 ms. When considered individually, the AVD associated with the largest stroke volume, was 100 ms in 2 patients and 140 ms in the remaining 5. At this individual optimal AVD the ventricular septal contraction occurred 31 +/-14 ms, before the end of the transmitral flow. The optimal AVD is, therefore, the one which synchronizes the ventricular and atrial systole so that the first ventricular septal contraction occurs after the peak of the A wave, just before the end of the transmitral flow. Because of the different functional cardiovascular status of the single patient, this parameter should be individualized, this can be clinically important as it may lead, in this patient population, to an improvement of the stroke volume up to 42% (Leonelli *et al.*, 1997).

Interatrial conduction blocks can be managed in some cases by proper programming of conventional DDD systems (Parravicini *et al.*, 2000). Kubica *et al.* (1993) found statistically significant difference between stroke volume with various atrioventricular delays. During pacing rate of 70 ppm the maximal difference was 19 and 15% during 100 ppm. Comparing both pacing rates the distributions of hemodynamically optimal atrioventricular delays was also significantly different. The best atrioventricular delay from the hemodynamic point of view

was 36 ms longer during 70 ppm of pacing rate than during 100 ppm. The most often optimal delay at 70 ppm was 190-200 ms and the rarest optimal delay was 90-100 ms, during 100 ppm pacing, respectively: 140-150 ms and 240-250 ms. We have observed considerable personal variability in the hemodynamic response for atrioventricular delay changing as well as in the hemodynamically optimal values of this parameter during both pacing rates. In this study, Atrioventricular delay programming has significant influence on left ventricular stroke volume. Programming of atrioventricular delay should be performed individually in every patient because of personal variability of optimal values of this parameter (Kubica *et al.*, 1993).

We found different optimal AVDs according CO, FT and MPI. Also, we concluded that Co derived optimal AVD is significantly higher than FT derived optimal AVD. So, what is the best method for optimization of AVD?

Analysis of parameters including IRT/ET and ICT/E as the components of MPI showed that there is not significant difference between CO, MPI and FT derived ICT/ET in optimal AVD. Also, the IRT/ET time in optimal AVD according the CO, MPI and FT is similar.

Because the main function of the heart is maintenance of sufficient CO for metabolic requirements of tissues, it seems that determination of optimal AVD according the highest CO, to be the gold standard method. However, our findings showed that the optimal AVD according the highest CO makes the highest CO, but it does not improve the diastolic function. Analysis of systolic intervals by using echo-Doppler showed that: determination of Co derived optimal AVD is in basis of a long ET with a short ICT and a long IRT, determination of FT derived optimal AVD is in basis of a short ET with a short ICT and a short IRT and determination of MPI derived optimal AVD is in basis of a long ET with a short ICT and a short IRT.

CONCLUSION

Different methods indicate different optimal AVDs. However, analysis of systolic and diastolic performance shows that different AVDs result in similar systolic or diastolic performance. At MPI optimized AVD, a high CO combined with the most advantageous conditions of both isovolumic contraction and relaxation phases is achieved.

Regarding the importance of AV interval in CO of patients with implanted DDD PM, it is recommended that following DDD and also in patients with PM syndrome, PM analysis to be performed in combination with echocardiographic assessment.

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