

Optimizing the Atrioventricular Delay in Dual Chamber Pacemakers; Is It Worth?

Abstract

Background: The number of patients treated with a dual chamber (DDD) pacemaker is continually increased each year. The Optimal AV synchrony will not only maximize cardiac output by increasing ventricular preload, thus lowering mean atrial pressure, but it will also minimize the diastolic mitral regurgitation. Until now, individualized optimization of the AVI is not performed in the clinical routine. This is mainly because of the time-consuming process of manual optimization and the lack of guideline recommendations.

Objective: To assess the optimal AV delay for each patient and to decide whether this optimization is worth doing it for all patients.

Patients and methods: After approval of Local Ethics Committee and obtaining written informed consent, a prospective, comparative randomized study was conducted on 56 patients with symptomatic bradyarrhythmia requiring dual chamber pacemaker implantation. All patients were assessed by thorough history taking, clinical examination, 12 lead surface ECG, and Echocardiography. They were randomly divided into two groups. Group A (28 patients): where their AVD was set at the default values, while in group B the AVD was optimized with guidance of the trans-mitral Doppler waves on echocardiography. Then echocardiography follow up was done after 12 months.

Results: Statistically significant increase was found in the LVEF in group B from 67.71 ± 4.58 to 73.43 ± 4.74 ($p < 0.0001$) while it was found to decrease in group A from 72.21 ± 6.28 to 69.43 ± 5.41 after 12 months of device implantation ($p < 0.0001$). Similar results were observed as regard the RVEF which decreased non significantly in group A after 12 months from 49.0 ± 5.82 to 48.07 ± 5.13 ($p: 0.07$), while in group B a significant increase from 48.57 ± 5.1 to 53.14 ± 7.31 was observed ($p < 0.0001$). Confirming these results again by analyzing the total change in LVEF and RVEF after one year and comparing the two groups directly. Both LVEF and RVEF show a highly significant increase in group B in comparison with group A ($P < 0.0001$). Also the LAP decreased significantly in both groups ($P < 0.001$).

Conclusion: Optimizing the AVD for all patients of DDD pacemakers may lead to long term beneficial effects mainly on the systolic functions.

Keywords: Pacemakers; DDD; Atrioventricular delay

Abbreviations: AV: Atrio-Ventricular; AVD: Atrio-Ventricular Delay; AVI: Atrio-Ventricular Interval; CO: Cardiac Output; CRT: Cardiac Resynchronization Therapy; DDD: Dual Chamber Pacemaker with Dual Pacing-Dual Sensing-Dual Response to Heart Rate; ECG: Electrocardiogram; EF: Ejection Fraction; IQR: Interquartile Range; LA: Left Atrium; LAP: Left Atrial Pressure; LV: Left Ventricle; LVEDD: Left Ventricular End Diastolic Dimension; LVEF: Left Ventricular Ejection Fraction; LVESD: Left Ventricular End Systolic Dimension; Ms: Milliseconds; NYHA: New York Heart Association; RV: Right Ventricle; RVEF: Right Ventricular Ejection Fraction; SD: Standard Deviation; TDI: Tissue Doppler Image

Introduction

The hemodynamically optimal delay programmed is dependent on the interval between LA and LV contraction; which in

turn is subject to the interatrial conduction delay [1]. The Optimal AV synchrony will not only maximize cardiac output by increasing ventricular preload; thus lowering mean atrial pressure; but it will also minimize the diastolic mitral regurgitation [2].

The usual nominally programmed A-V intervals in a DDDR pacemaker; 125 to 175 msec; May not provide the optimal AV synchrony at these patients; and AV delays as long as 250 to 350 msec may be required [1]. Currently; individualized optimization of the AVI is not performed in the clinical routine. This is mainly because of the time-consuming process of manual optimization and the lack of guideline recommendations [3,4].

Here in; we aimed in this study to optimize the AVD in patients with an implanted DDD pacemaker and to compare the systolic and diastolic performance between the optimized AVD and the default AVD of the manufacturer; as well as to assess the optimal

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Jane Aboulenein^{1*}, Mazen Tawfik²,
Abdelrazek Maaty¹, Hesham Wali¹ and Wael
Refaei¹

¹Cardiology Department, Mansoura University, Egypt

²Professor of Ain Shams University, Egypt

***Corresponding author:** Jane Aboulenein, Cardiology Department, Faculty of Medicine, Mansoura University, Egypt, Tel: +20-10-19025804; Fax: +20-50-2267016; Email: cardiolojane@gmail.com

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AV delay for each patient and to decide whether this optimization is worth doing it for all patients.

Materials and Methods

Study population

Fifty six patients were enrolled in this study; (mean age was 58.11 ± 15.17 years; 24 males) with an initial dual chamber pacemaker implanted for complete heart block in 50 patients and other indications were found in 6 patients.; 12 were diabetic patients; 24 were hypertensive and all had their DDD pacemakers implanted in Mansoura specialized medical hospital over a period of 3 years from October 2012 to October 2015.

Ethics statement

All procedures were performed as recommended by the guidelines and during implantation and during the routine pacemaker follow-up. Data was analyzed anonymously. The study was explained to all patients and they gave oral informed consent. Besides; the study is approved by the ethics committee of the Faculty of medicine; Mansoura University.

Methodology

56 patients were enrolled in this study; (mean age was 58.11 ± 15.17 years; 24 males) with an initial dual chamber pacemaker implanted for complete heart block in 50 patients and other indications were found in 6 patients; 12 were diabetic patients; 24 were hypertensive and all had their DDD pacemakers implanted in Mansoura specialized medical hospital over a period of 3 years from October 2012 to October 2015.

For each patient a complete medical history was taken; including a detailed inquiry of onset of symptoms related to heart block; how the patient discovered to be affected. When possible electrocardiographic tracings previous to the occurrence of the block were examined. History including fine analysis of symptoms such as syncope and/or dizziness; all patients were in NYHA functional class I.A complete physical examination was done with particular attention to the cardiovascular and respiratory systems. Plain postero-anterior; standing; chest X ray was done for all patients to determine heart size; cardiac shadow configuration; pulmonary vascularization and if any pulmonary pathology is present. A basal standard 12 leads electrocardiogram was done for each patient to confirm the diagnosis and to document it; to assess QRS configuration and width; and to detect the presence of any other abnormality or arrhythmias.

Exclusion Criteria: Patients with EF less than 60% were excluded from the study.

Intervention: All devices were introduced through the left subclavian vein; the atrial lead was set in the right atrial appendage while the ventricular lead was placed in the right ventricular apex in all patients. The procedures were done in the Specialized Medicine Hospital in Mansoura University. The devices were randomly selected as regards the manufacturer's brand; including Biotronik; Boston Scientific; Medtronic and St. Jude.

Echocardiography

All patients have had a preoperative echography using a commercially available device (General Electric; Vivid 5S) with more stress on the following:

- Pulsed wave Doppler on the mitral valve inflow to determine the peak and shape of both E and A waves and the amount of mitral regurgitation (if any).
- Left ventricular ejection fraction (LVEF) via measuring the LV dimension at the end diastole (LVEDD) and end systole (LVESD). LVEF was measured using the M mode.
- Right ventricular ejection fraction (RVEF) either by Simpson method or subjectively by eyeballing.
- The peak velocity average of myocardial shortening (S_m) and the peak velocity average of early myocardial relaxation (E_m); using tissue Doppler index (TDI) in the apical 4 chamber view by placement of a 3-mm sample volume at the lateral and septal mitral annulus and also the tricuspid annulus septally and laterally.

After pacemaker implantation; the patients were randomized into two groups; 28 of the patients (control) where the atrioventricular delay (AVD) as the default parameters set by the manufacturer; the default value for the different brands was either 180/150ms or 150/120ms for the paced/sensed AVD respectively. While the other group (patient) had the AVD optimized by the echocardiography imaging where the optimum AVD will be the best transmitral flow and discrete E/A separation in the following steps:

- Paced AVD will be increased successively from 80 to 200 ms at 20 ms stepwise intervals (with respect to a less value of the sensed AVD by 30 ms).
- At each value; pulsed Doppler transmitral flow was recorded and compared with each other.
- The optimum AVD was agreed to be the value that showed:
- Good E-A separation (no fusion of the two waves).
- No (or the least) mitral regurgitation.
- No A wave truncation.
- Follow up visits were made every three months; until one year post implantation where in each visit the following steps were done:
- History taking (dyspnea; functional NYHA class; any symptoms of heart failure; arrhythmia).
- Echocardiography assessment to confirm optimization.
- The findings were compared after one year in each group; then the change after one year was again compared between the two groups.

Statistical analysis

The clinical and investigational data were recorded on an "Investigation report form". These data were tabulated; coded then analyzed using the computer program SPSS (Statistical package for social science) version 20 to obtain:

Descriptive statistics were calculated for the anthropometric measurements in the form of:

- a. Mean ± Standard deviation (SD).
- b. Median and range (Minimum – Maximum).
- c. Frequency (Number-percent).

Analytical statistics in the statistical comparison between the different groups; the significance of difference was tested using one of the following tests:-

- i. Student’s t-test: used to compare between mean of two groups of numerical (parametric) data.
- ii. Mann-Whitney U-test: used to compare between two groups of numerical (non-parametric) data.

A P value <0.05 was considered statistically significant.

Results and Discussion

The study included 56 patients where the mean age was 58.11± 15.17 y; all demographic parameters and basal echocardiographic measurements are plotted in Table 1.

Table 1: Shows average results of the study population.

Age (mean±SD)		58.11±15.17	
Gender (male)		24	42.86%
INDICATION	CHB	44	78.50%
	Post-operative CHB	6	10.70%
	OTHERS	6	10.70%
Hypertension		24	42.80%
Diabetic		12	21.40%
LVEF (mean±SD)		69.96±5.89	
RVEF (mean±SD)		48.79±5.43	
PEAK_E (median-IQR)		1.1	1.46
MITRAL_E' (median-IQR)		0.07	0.06
E_E (median-IQR)		22.33	74.25
LAP (median-IQR)		29.59	92.07

SD: Standard Deviation; IQR: Interquartile Range; LVEF: Left Ventricular Ejection Fraction; RVEF: Right Ventricular Ejection Fraction; LAP: Left Atrial Pressure.

All patients had symptoms only related to the bradycardia caused by the heart block; such as dizziness; easy fatigability; exertional dyspnea and sporadic syncopal attacks. On performing echocardiography to all patients; the LVEF averaged 69.96 ± 5.89 while the RVEF was 48.79 ± 5.43; the other parameters were

non parametric where the peak E showed a median of 1.1 and IQR of 1.46; from the tissue Doppler data the E' of the lateral mitral annulus recorded a median of 0.05 and IQR 0.06; whereas the mitral E/E' ratio was of a median 22.33 and IQR 74.25. We calculated the left atrial pressure (LAP) from the Nagueh formula $1.9 + (1.24 \times E/E')$ [5] which measured a median of 29.59 and IQR of 92.07. This data was then separated for each group. After dual chamber pacemaker implantation; the patients were randomized into two groups; group 'A' which is the control group where the AVD was programmed as default values set by the manufacturer while the second group 'B' where the AVD will be optimized; follow up visits and echocardiographic study was done every three months to assure optimization and the findings were compared after one year in each group; then the change after one year was again compared between the two groups.

The LVEF was found to decrease in group A from 72.21±6.28 pre implantation to 69.43±5.41 after 12 months (p<0.0001); while in group B the LVEF increased from 67.71±4.58 to 73.43±4.74 (p<0.0001)

Similar results were observed as regard the RVEF which decreased non significantly in group A after 12 months from 49.0±5.82 to 48.07±5.13 (p: 0.07); while in group B a significant increase from 48.57±5.1 to 53.14±7.31 was observed (p<0.0001).

These results were again confirmed by analyzing the total change in LVEF and RVEF after one year and comparing the two groups directly. Both LVEF and RVEF show a highly significant increase in group B in comparison with group A (P<0.0001) as illustrated in Figure 1. We calculated the left atrial pressure (LAP) from the Nagueh formula $1.9 + (1.24 \times E/E')$ [5] where a significant reduction in the LAP was recorded in both group A (p: 0.001) and group B (P<0.0001). Comparing between the two groups as regard the change in LAP concluded a non significant difference across the 2 groups after one year (p: 0.81) (Figure 2).

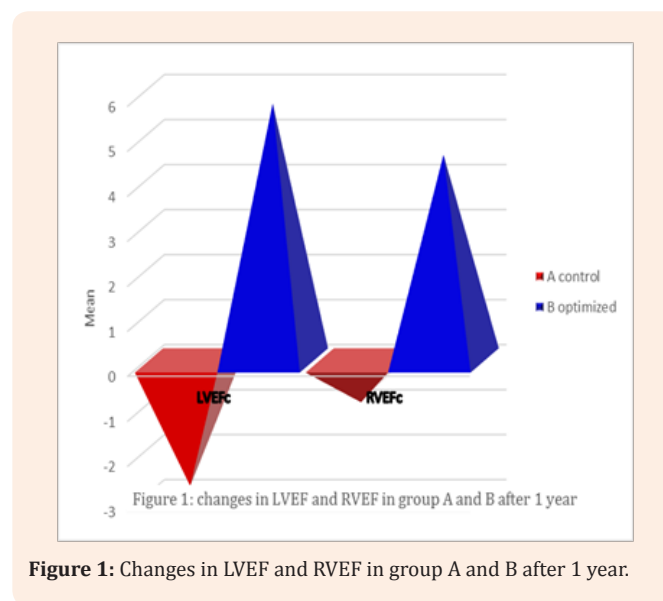


Figure 1: Changes in LVEF and RVEF in group A and B after 1 year.

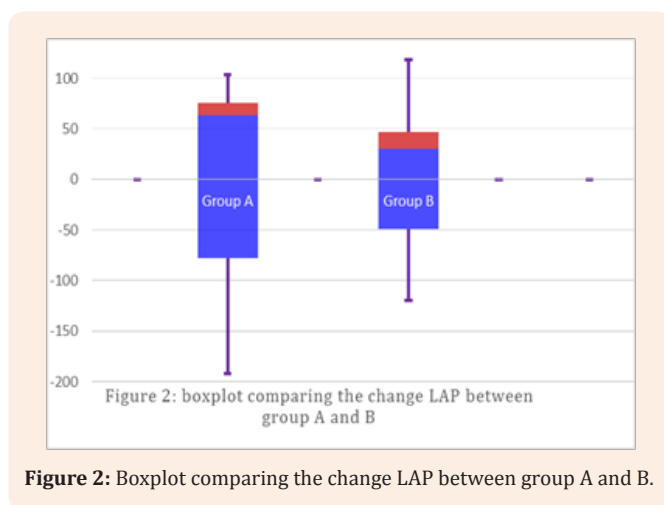


Figure 2: Boxplot comparing the change LAP between group A and B.

Discussion

The AVD is the time from the beginning of paced or sensed atrial activity to the impulse of ventricle stimulation or sensed ventricular activity. Modern DDD pacemakers allow a wide range of programming of AVD and AVD-related algorithms [6]. Proper setting of AVD allows to achieve electromechanical synchrony of atrial and ventricular contractions and the individual setting of AVD in patients with atrio-ventricular block can have the beneficial effects not only on the contractile function of the heart; but also on long-term prognosis [7]. Too short AVD results in initiation of ventricular contraction during atrial systole and hence abbreviates atrial systole and results in underfilling of the ventricle [8,9]. Too long AVD causes diastolic mitral regurgitation; both of which can reduce CO [8,9]. Echocardiography has been used in the optimization of AVD in patients with DDD pacemaker for more than 10 years [10]. Several methods have been suggested to find optimal AVD. Several studies from single centers have shown improvement in cardiac output by echo Doppler-guided AVD optimization [11-13]. Doppler parameters used for echo-guided optimization include aortic VTI [14,15]; diastolic mitral flow pattern by Ritter's method [16]; iterative method [17]; diastolic filling time [13]; VTI of mitral inflow [18]; Doppler-derived dP/dt [7]; tissue Doppler imaging [11,12]; LV and right ventricular (RV) pre-ejection delays; and myocardial performance index [19].

Our study proved a significant improvement in the ejection fraction of the left ventricle and this is supported by some researchers as follows:

In 2008; Patrick Seigrist proved an improvement in the LVEF after optimizing CRT devices and they correlated this improvement only to the atrio ventricular synchrony obtained by the AVD optimization [20].

In addition to that; a regional population study in Romania was performed on patients with DDD pacemakers; the study showed a significant improvement in the left ventricular ejection fraction after optimizing the AVD through an ECG dependent algorithm [21].

On the contrary; Ellenbogen [22] claimed that either manual optimization or the automated algorithms have no significant impact on the systolic functions.

Ellenbogen gave different explanations to this odd result in comparison to many other published results; one of these explanations is that there may be a hemodynamic benefit but it runs in a small range to give a significant statistical value and this may be a result of the baseline condition of the patients sent for a CRT device implantation; which is not the condition in our study. Moreover; Kerlan [14] claimed 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 [14].

Chinese group [23] also observed a significant improvement in the LVEF after optimizing the AVD using a specific ECG algorithm. It is obvious that all of the above mentioned studies went after detection of acute results after optimizing the AVD; except for one study [22] which measured the change in hemodynamics for a period of 6 months post implantation of CRT devices. We followed the patients for 12 months to detect the long term benefit of optimization and the results point to permanent benefits for the patients of dual chamber pacemaker.

Recently in the year 2015; Koneru [24] proved an improved diastolic function and lower atrial filling pressures with an Echo-Guided AV optimization [24]. In comparison to our work; we could prove a significant improvement in diastolic functions of the LV as well as significant reduction in the LAP in the AVD optimized group; however the results were not significantly different from the control group; improvement of diastolic function should be mainly attributed to the resolution of the cannon A wave and bradycardia which was the case before pacemaker implantation. A dual chamber pacemaker should be supposed to illicit some sort of AV communication which might be helping to decrease the LAP and improve diastolic function.

Surprisingly; none of the previous studies involved the assessment of the RV systolic function; we included studying the RVEF using the Simpson's method or in some times by observation (eyeballing method); and a significant improvement in the RVEF was noticed in the AVD optimized group. To explain this; the same as it is the case for the LV; the optimal AV interval should allow completion of end-diastolic filling of the RV prior to ventricular contraction. An appropriately timed atrial systole improves the right ventricle filling and hence the stroke volume or cardiac output of the RV by means of the Starling law.

Conclusion

This work has ended up agreeing that it is very wise to put all patients of DDD pacemakers for AVD optimization as this may help long term beneficial effects mainly on the systolic functions.

Study limitations

Several potential limitations of the mitral inflow method for AV delay optimization may have compromised the performance

of this method. For example; the mitral inflow method is critically dependent on visualizing mitral A wave truncation as a result of premature mitral valve closure with a very short AV delay. In patients with LV diastolic dysfunction; a common occurrence in heart failure patients; the mitral A wave may be severely attenuated or abbreviated by early mitral valve closure. Therefore; performance of the mitral inflow method may be compromised in these patients.

This study is also limited by the small number of patients enrolled. We did not measure other echocardiographic parameters the strain and strain rate. We are proposing to develop our study using more detailed echocardiographic findings

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