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ORIGINAL RESEARCH ARTICLE

Effects of optimized left atrioventricular conduction time on hemodynamics and prognosis in patients with third degree atrioventricular block implanted with dual chamber pacemakers

Shulan Zhang[1], Jiaqi Qiang[1], Qingxiong Yue[2], Linan Li[2], Peishi Yan[3], Jing Dong[1], Jie Qiao[1], Hailong Lin[3,*]

[1] *Department of Cardiac Electrophysiology, Dalian Municipal Central Hospital Affiliated of Dalian Medical University, Dalian 116033, Liaoning, China*

[2] *Department of Ultrasonography, Dalian Municipal Central Hospital Affiliated of Dalian Medical University, Dalian 116033, Liaoning, China*

[3] *Department of Cardiovascular Medicine, Dalian Municipal Central Hospital Affiliated of Dalian Medical University, Dalian 116033, Liaoning, China*

*** Corresponding author:** Hailong Lin, Indllhl2018@163.com

ABSTRACT

Objective: To investigate the effect of optimized left atrioventricular conduction time (Lavi) on hemodynamics and prognosis of patients with third degree atrioventricular block implanted with dual chamber pacemakers. **Methods:** 120 patients with third degree atrioventricular block implanted with dual chamber pacemaker were randomly divided into Lavi optimized group and non optimized group. Oesophageal electrocardiography was performed 3 months after pacemaker implantation (observation base point). The atrial conduction time (IACT) and interventricular conduction time (IVCT) of the two groups were measured and the Lavi under the default atrioventricular delay (AVD) state of the pacemaker was calculated. The optimization group then adjusted the AVD of the pacemaker under the guidance of echocardiography to obtain the optimal Lavi under the best mechanical synchronization state of the left atrioventricular. All patients were examined by echocardiography at 6, 12 and 18 months after operation. ECG conduction parameters, related clinical manifestations and prognostic indicators were observed, and the relationship between optimal Lavi and heart rate was analyzed. **Results:** a) In the optimization group, the average optimal Lavi was (130.8 ±11.9) ms, which was longer than the default Lavi value (120.7 ±18.7ms) ($p < 0.05$). b) In the optimization group, the optimal Lavi was negatively correlated with heart rate ($r = -0.955$, $p < 0.05$), heart rate <70 beats/min, and the optimal Lavi was 140 ms; the heart rate was 70~80 beats/min, and the optimal Lavi was 130ms; heart rate >80 beats/min, and the optimal Lavi is 120 ms. c). Optimization of Lavi could immediately improve e-peak deceleration time (EDT) and isovolumic relaxation time (IVRT) in the optimization group ($p < 0.05$). d) The left ventricular ejection fraction (LVEF), EDT and IVRT of the optimized group were better than those of the non optimized group at 6 months after operation ($p < 0.05$), and the left atrial volume index and e/e '(the ratio of early diastolic flow velocity of mitral orifice to early diastolic movement velocity of mitral annulus) were better than those of the non optimized group at 12 months after operation ($p < 0.05$). e) LVEF and EDT in the non optimized group decreased gradually during the follow-up period of 18 months ($p < 0.05$); IVRT and left atrial volume index increased gradually during the whole follow-up period ($p < 0.05$). E/e 'in the optimization group increased gradually during the follow-up period ($p < 0.05$), while EDT decreased gradually during the follow-up period ($p < 0.05$). f) The cumulative incidence of new paroxysmal atrial fibrillation in the optimization group was significantly lower than that in the non optimization group (8.3% vs. 23.3%, $p < 0.05$). Conclusion optimization of Lavi can improve hemodynamics and reduce the incidence of atrial fibrillation in patients with third degree atrioventricular block implanted with dual chamber pacemakers.

Keywords: cardiology; left atrioventricular interval; pacemaker; atrioventricular block; cardiac function; prognosis

1. Introduction

Atrioventricular synchronization, especially the synchronization between left atrium and left ventricle, is the main part of cardiac motion synchronization, which has a significant impact on the electrical and mechanical functions of the heart[1,2]. The decrease of left atrioventricular synchronization can induce the decline of cardiac function and increase the risk of atrial fibrillation (AF). Left atrioventricular synchronicity is mainly affected by left atrioventricular conduction time (Lavi). Theoretically, too long or too short Lavi will reduce left atrioventricular synchronicity[3]. Patients with third degree atrioventricular block can be implanted with dual chamber pacemakers to maintain the sequential contraction of atrioventricular, but pacing of right atrioventricular and right ventricle will significantly change the electrical conduction of the heart, which may lead to long or short conduction time of left atrioventricular and reduce the mechanical synchronization of left atrioventricular. In addition, other coexisting factors, such as the change of heart rate, may also affect the left atrioventricular mechanical synchronization under pacing. Because it is difficult to determine Lavi by body surface ECG, the author used the left atrioventricular mechanical synchrony monitored by echocardiography as a references standard, and with the help of esophageal ECG recording technology, optimized Lavi by adjusting atrioventriculardelay (AVD) of dual chamber pacemaker, to explore the impact of optimized Lavi on the clinical prognosis of patients with third degree atrioventricular block after implantation of dual chamber pacemaker.

2. Data and methods

2.1. Research object

120 patients with dual chamber pacemakers were selected from January 2017 to June 2019. The implanted pacemakers are DDD (R) pacemakers produced by Medtronic, and the initial AVD and lower limit pacing frequency are set by the default of the pacemaker factory [pacing atrioventricular interval (PAV) 150 ms, perceived atrioventricular interval (SAV) 120 ms; lower limit frequency: 60 times/min], and the starting sleep frequency (50 times/min). This research plan was approved by the ethics committee of the hospital (ethics approval No.: Lunshen scientific research 2017-031-10).

Grouping:

The patients were randomly divided into Lavi optimized group and Lavi non optimized group, with 60 cases in each group. Taking the main interval of the whole day heart rate distribution in the heart rate histogram stored by the pacemaker as a reference, the Lavi optimization group was divided into: Low heart rate group: 50 beats/minute < heart rate <70 beats/minute, central rate group: 70~80 beats/minute, high heart rate group: 80 beats/minute < heart rate <100 beats/minute.

Inclusion criteria and exclusion criteria:

Inclusion criteria: a) Persistent third degree atrioventricular block; b) first implantation of dual chamber

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pacemaker; c) the atrial electrode was placed in the right atrial ear, and the ventricular pacing spiral electrode was placed in the right ventricular septum. Exclusion criteria: a) Preoperative history of atrial fibrillation; b) severe heart valve disease; c) preoperative cardiac insufficiency NYHA III–IV; the cardiac function was NYHA II–IV at 3 months after operation; d) severe cardiomyopathy; e) malignant tumor; f) severe pulmonary disease, endocrine disease, severe liver and kidney dysfunction, etc.; g) there are contraindications of esophageal electrocardiogram.

2.2. Method

Observation time point and operation:

The selected time point 3 months after pacemaker implantation was taken as the observation base point, and 6, 12 and 18 months after pacemaker implantation were taken as the follow-up observation time points. At the observation base point, the general demographic data and general clinical manifestations of the patients were recorded, and the esophageal ECG and echocardiography were performed. In the Lavi optimization group, the pacemaker was programmed and optimized under the guidance of echocardiography, and the echocardiographic parameters before and after optimization were recorded; at each follow-up observation time point, cardiac echocardiography was rechecked, and NYHA cardiac function changes, syncope, cardiac death, all-cause death, cardiac readmission and pacemaker parameters were recorded.

General clinical data:

Including: Gender, age, smoking history, combined diseases such as hypertension, diabetes, chronic cardiac insufficiency, coronary heart disease, etc., and the proportion of pacemaker atrial pacing; syncope and NYHA cardiac function classification.

Esophageal electrocardiogram:

The test was completed by the same electrophysiologist, and the instrument used was the new cardiac electrophysiological stimulator DF-5A. Detection method: The 5-pole esophageal electrode catheter is inserted into the esophagus through the nasal cavity, and the estimated insertion depth (CM) = (height of the subject + 200)/10 + 3. After the catheter reaches the depth, the position of the electrode catheter is further fine adjusted to make the esophageal lead record the high P wave[4], and the body surface 12 lead and esophageal lead synchronous ECG under the sinus rhythm and pacing rhythm (the pacing heart rate is adjusted to be higher than and closest to the sinus heart rate), Measure the interatrialconductiontime (IACT), IACT for atrial sensing ventricular pacing (iacts), and IACT for dual chamber pacing (iactp). Continue to probe the electrode catheter (about 2~5cm) until the esophageal lead clearly shows the left ventricular depolarization wave. Measure the interventionalconductiontime (IVCT), as shown in **Figure 1**. Based on this, calculate Lavi, LAVI = AVD-IACT + IVCT.

Echocardiography:

It was completed by the same ultrasound diagnostic physician, and the instrument was Philips ieelit color Doppler ultrasound diagnostic instrument. The patient was resting for 10min before the test. Outcome measures: a) Left ventricular ejection fraction (LVEF); b) left ventricular diastolic function: Early diastolic flow velocity (E), late diastolic flow velocity (a), peak decelerationtime (EDT), early diastolic motion velocity (e’) of mitral annulus, isovolumicrelationtime (IVRT); c) Leftatrialvolume (LAV). The above data were measured continuously for 5 cardiac cycles, and the mean value was obtained through calculation: Left atrial volume index, e/e’. The echocardiographic results of Lavi optimization group before optimization were baseline echocardiographic parameters.

(a) **(b)** **(c)**

Figure 1. Measurement of transetrial and interventricular conduction time of esophageal electrocardiogram. **(a)** is iacts 60 ms; **(b)** is iactp 110 ms; **(c)** is IVCT 48 ms during dual chamber pacing.

Lavi optimization:

Lavi optimization is performed at the observation base point. In the optimization group, the AVD (PAV or SAV) of pacemaker was adjusted under the guidance of echocardiography based on the main interval of whole day heart rate distribution, and the optimal mechanical synchronization of left atrium and ventricle was achieved. The conversion relationship between the optimal PAV and SAV was: Pav = sav + (iactpiacts) (the calculation results were rounded to ten). Then calculate the Lavi in this state as "optimal Lavi". The standard for the best mechanical synchronization of left atrium and ventricle: The total duration of peak e + peak a in the mitral flow spectrum reaches the longest without peak a tailoring[5] (as shown in **Figure 2**). See **Figure 3** for the comparison of mitral flow spectrum before and after optimization.

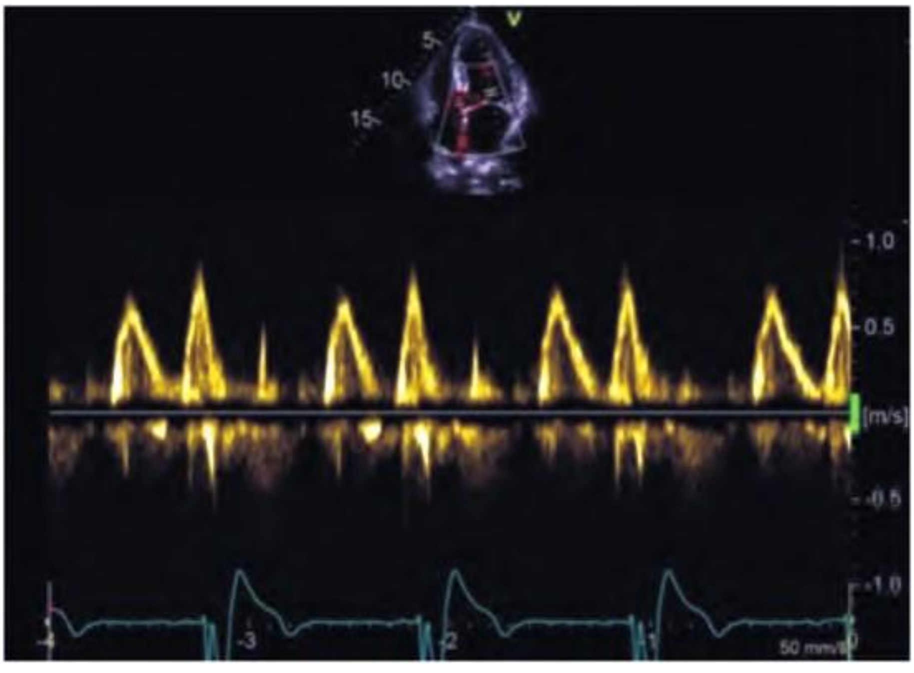

Figure 2. Echocardiographic mitral flow spectrum of sinus rhythm 60 beats/min right ventricular pacing. When sav = 140 ms, lavi = 140 ms, echocardiographic measurement indicators: Lvef 0.62, edt 190.3 ms, IVRT 114 ms.

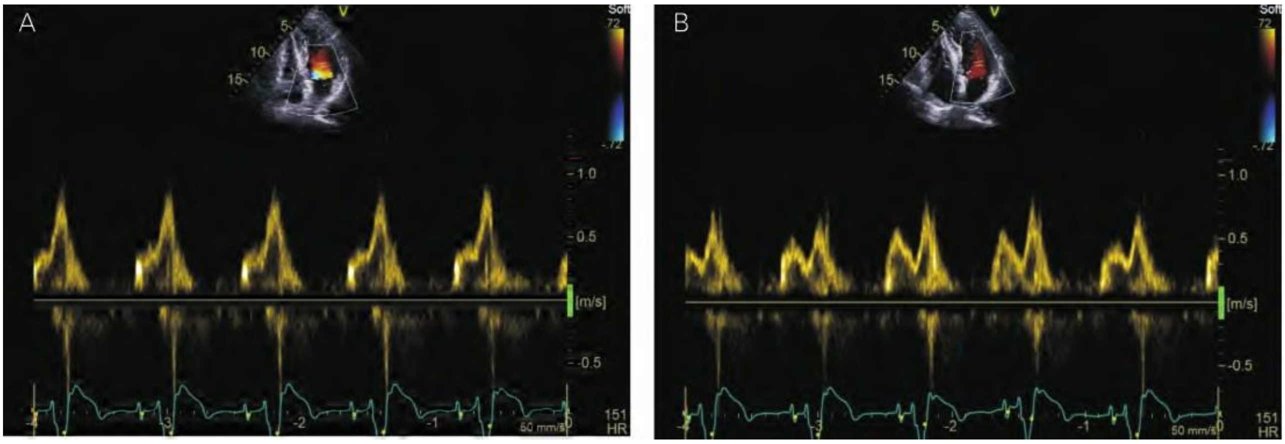

Figure 3. Echocardiographic mitral flow spectrum before and after dual chamber pacing 75 times/min and optimization of Lavi. **(A)** partial fusion of e-A peak can be seen when pav = 150 ms and lavi = 166 ms; **(B)** when pav = 110 ms and lavi = 126 ms, the overlap ratio of e-A peak decreases significantly.

The indexes of echocardiography before and after optimization were recorded. The Lavi of patients in the non optimization group was measured by esophageal ECG under the pacemaker factory default AVD state. Since IACT is relatively fixed when there is no significant change in heart rate[6], iacts, iactp and IVCT are not compared before and after optimization, and are regarded as fixed values.

Other follow-up data:

Collection of atrial fibrillation events: Atrial fibrillation events were recorded when the central atrial rate of atrial high-frequency events stored by pacemakers was >350 times/min, and those with a duration of <48 h were recorded as paroxysmal atrial fibrillation. Cardiogenic readmission and death events: Including readmission and death caused by angina pectoris, cardiomyopathy, myocardial infarction, heart failure, cardiogenic embolism and arrhythmia. One patient with multiple positive events was recorded.

2.3. Statistical analysis

SPSS 26.0 software is adopted. Counting data are expressed by use cases or percentages, and the difference between groups is expressed by chi square test or Fisher exact probability method; the measurement data conforming to the $\bar{x} \pm s$ normal distribution is represented by two independent samples *t*-test; the data with abnormal distribution were expressed by the median *m* (P25, p75), and the rank sum test was used. The correlation between optimal Lavi and heart rate was analyzed by Spearman method. The difference was significant ($p < 0.05$).

3. Results

3.1. General clinical data of two groups of patients

See **Table 1** for comparison of general clinical data.

Table 1. Comparison of general clinical data between the two groups.

Group	*n*	Male/female	Age/year	Smoking history/case	Hypertension/ case	Diabetes/case	Chronic cardiac insufficiency/case	Coronary heart disease/case	Atrial pacing ratio/%
Lavi optimization group	60	26/34	73.8 ± 9.7	9 (15%)	40 (66.7%)	16 (26.7%)	9 (15%)	13 (21.7%)	22.8 (6.5, 36.8)
Lavi non optimization group	60	31/29	72.2 ± 12.3	10 (16.7%)	32 (53.3%)	17 (28.3%)	6 (10%)	10 (16.7%)	19.9 (8.0, 33.6)
P		0.465		0.444	1.000	0192	1.000	0.582	0.643

3.2. Comparison of ECG parameters measured at the observation base point between the two groups and optimization of Lavi optimization group

There was no difference in ECG parameters measured at the observation base point between the two groups ($P > 0.05$). See **Table 2.** After optimization, PAV and lavip in the optimization group were significantly longer than those before optimization [160.2 ± 22.8 msvs 150 ms; (130.8 ± 11.9) msvs (120.7 ± 18.7) ms, $P < 0.05$], and SAV and Lavis had no significant difference compared with those before optimization [123.3 ± 22.4 msvs 120 ms; (130.8 ± 11.9) msvs (127.6 ± 17.9) ms, $P > 0.05$].

Table 2. Comparison of ECG parameters measured by baseline esophageal ECG records between the two groups/ms.

Group	*n*	Iacts	Iactp	IVCT	SAV	PAV	Lavis	Lavip
Lavi optimization group	60	59.6 ± 9.2	96.5 ± 12.2	67.2 ± 16.7	120	150	127.6 ± 17.9	120.7 ± 18.7
Lavi non optimization group	60	59.6 ± 9.8	93.5 ± 8.9	68.3 ± 9.9	120	150	128.8 ± 14.4	124.8 ± 13.8
P		0.970	0.127	0.651			0.686	0.170

The heart rate of patients in the optimization group was negatively correlated with the optimal Lavi ($r = -0.955$, $p < 0.05$), and the linear fitting formula was $y = -1.332x + 228.6$, $r2 = 0.8831$. The average value of the optimal Lavi of all patients in the optimization group was [(130.8 ± 11.9)(86~152)] ms; after optimization, the average value of sav was (123.33 ± 22.37) ms, and the average value of PAV was (160.17 ± 22.81) ms. The optimal Lavi of low heart rate group ($n = 22$) was [(142.1 ± 5.1)(130~152)] ms, that of center rate group ($n = 25$) was [(128.6 ± 5.1)(114~138)] ms, and that of high heart rate group ($n = 13$) was [(116.0 ± 11.1)(86~124)] ms. The optimal Lavi was 140 ms for 73% of patients in the low heart rate group, 130 ms for 80% of patients in the center rate group, and 120 ms for 77% of patients in the high heart rate group.

3.3. Comparison of echocardiographic parameters between the two groups

In the Lavi optimization group, EDT and IVRT were improved immediately ($P < 0.05$), as shown in **Table 3**. There was no significant difference in echocardiographic parameters between optimized group and non optimized group ($P > 0.05$); at the following follow-up points, the echocardiographic parameters in the optimization group gradually showed continuous improvement compared with those in the non optimization group ($P < 0.05$). See **Tables 4** and **5**.

Table 3. Comparison of echocardiographic parameters of Lavi optimization group before and after optimization 3 Months after operation.

Group	*n*	LVEF	EDT/ms	IVRT/ms	Left atrial volume index	E/e′
Before optimization	60	0.58 ± 0.06	125.1 ± 29.2	133.6 ± 23.6	34.9 ± 5.6	13.9 ± 2.1
After optimization	60	0.60 ± 0.05	146.1 ± 34.4	118.8 ± 21.4	33.2 ± 5.1	13.2 ± 2.5
P		0.105	0.000	0.000	0.091	0.080

Table 4. Baseline and LVEF during follow-up of patients in Lavi optimization group and non optimization group.

Category	LVEF			
	3 months	**6 months**	**12 months**	**18 months**
Lavi optimization group	0.58 ± 0.06	0.60 ± 0.05	0.59 ± 0.05	0.58 ± 0.03
Lavi non optimized group	0.58 ± 0.04	0.57 ± 0.04	0.56 ± 0.05	0.54 ± 0.06
P	0.698	0.006	0.005	0.000

Table 5. Observation base points and echocardiographic parameters during follow-up of patients in Lavi optimization group and non optimization group.

Category	EDT/ms				IVRT/ms			
	3 months	6 months	12 months	18 months	3 months	6 months	12 months	18 months
Lavi optimization group	125.1 ± 29.2	145.0 ± 27.4	136.1 ± 32.0	132.0 ± 20.5	133.6 ± 23.6	114.7 ± 22.7	120.2 ± 21.1	122.1 ± 15.3
Lavi non optimization group	133.3 ± 35.6	125.2 ± 38.0	120.0 ± 29.3	110.5 ± 30.2	133.0 ± 29.2	138.9 ± 28.4	145.6 ± 31.7	148.2 ± 17.3
P	0.172	0.001	0.005	0.000	0.905	0.000	0.000	0.000
	34.9 ± 5.6	33.8 ± 4.5	34.0 ± 3.5	34.5 ± 2.9	13.9 ± 2.1	13.8 ± 2.6	14.0 ± 2.0	14.4 ± 2.2
	34.7 ± 4.5	34.8 ± 4.4	36.3 ± 4.3	37.3 ± 5.1	14.7 ± 2.5	14.7 ± 2.8	15.5 ± 3.0	15.7 ± 3.1
	0.860	0.204	0.002	0.000	0.086	0.064	0.000	0.011
Category	**Left atrial volume index**				**E/e'**			
	3 months	**6 months**	**12 months**	**18 months**	**3 months**	**6 months**	**12 months**	**18 months**
Lavi optimization group	34.9 ± 5.6	33.8 ± 4.5	34.0 ± 3.5	34.5 ± 2.9	13.9 ± 2.1	13.8 ± 2.6	14.0 ± 2.0	14.4 ± 2.2
Lavi non optimization group	34.7 ± 4.5	34.8 ± 4.4	36.3 ± 4.3	37.3 ± 5.1	14.7 ± 2.5	14.7 ± 2.8	15.5 ± 3.0	15.7 ± 3.1
P	0.860	0.204	0.002	0.000	0.086	0.064	0.000	0.011

At 6 months after operation, LVEF, EDT and IVRT in the optimized group were significantly better than those in the non optimized group ($P < 0.05$). This difference still existed at 12 and 18 months after operation; at 12 months after operation, the LAV index and e/e 'of the optimized group were also significantly better than those of the non optimized group ($P < 0.05$). This difference still existed at 18 months after operation. LVEF and EDT in the non optimized group decreased gradually during the follow-up period of 18 months ($P < 0.05$); IVRT and LAV index increased gradually during the whole follow-up period ($P < 0.05$). E/e 'in the optimization group increased gradually during the follow-up period ($p < 0.05$), while EDT decreased gradually during the follow-up period ($p < 0.05$); lvef decreased gradually during the 18 month follow-up period, but it did not reach statistical significance; however, IVRT and LAV indexes did not change during the whole follow-up period, as shown in **Tables 4** and **5**.

3.4. Changes of new onset atrial fibrillation and other clinical prognostic indicators

See **Table 6.** No all-cause death, cardiac death and syncope occurred in the two groups.

Table 6. Comparison of prognosis between the two groups/case.

Group	Cumulative number of patients with new onset atrial fibrillation				NYHA cardiac function classification (18 Months)			Cardiogenic readmission (18 Months)
	3 months	6 months	12 moths	18 months	I	Π	Ш	
Lavi optimization group	2 (3.3%)	2 (3.3%)	4 (6.7%)	5 (8.3%)	58	1	1	4 (6.7%)
Lavi non optimization group	1 (1.7%)	5 (8.3%)	7 (11.7%)	14 (23.3%)	56	3	1	8 (11.7%)
P	1.000	0.439	0.529	0.043	0.412			0.362

4. Discussion

Usually, the pacing electrodes of patients with dual chamber pacemakers are placed in the right atrial appendage and right ventricle. Right atrial pacing prolongs IACT, and right ventricular pacing makes left ventricular depolarization later than right ventricle. Both of them have a significant impact on Lavi[3]. In this study, when the pacemaker is right atrial pacing rather than right atrial sensing, it is necessary to appropriately extend PAV to obtain the best hemodynamic Lavi, indicating that right atrial pacing does significantly prolong IACT. At this time, only synchronously extending PAV can ensure the mechanical synchronization of left atrium and ventricle. Undoubtedly, when IACT and IVCT cannot be adjusted, adjusting AVD of pacemaker is the only way to obtain the optimal Lavi[7,8].

The pacemakers used in this study were all made by Medtronic. The factory default setting values of sav and PAV were 120 ms and 150 ms respectively. After adjusting AVD to obtain the optimal Lavi, the sav value basically did not change, but PAV increased significantly, indicating that the factory default setting value of pacemakers is generally reasonable, but pav is relatively short. Therefore, theoretically, it is reasonable to set the factory default setting value of PAV to 160ms found in this study. Of course, this fixed value setting of solidification can not meet the complicated individual changes in clinical practice, and it is necessary to carry out similar optimization in this study.

This study found that heart rate has a significant impact on the optimal Lavi. The optimal Lavi is inversely proportional to heart rate. The faster the heart rate, the shorter the optimal Lavi. This is because when the heart rate increases, the filling time of the left ventricle is shortened, and the time of Lavi must be appropriately shortened to ensure that the filling blood flow formed by left atrial contraction completely falls at the end of left ventricular diastole, that is, to ensure the filling mechanical coordination between the left atrioventricular[8]. This study shows that if the AVD of pacemaker is adjusted only based on the optimal Lavi of esophageal ECG, and the normal heart rate level range (60~100 beats/min) is roughly divided into three heart rate intervals to formulate the interval optimal Lavi standards, these standards are: Heart rate <70 beats/min, the optimal Lavi is 140ms; the heart rate was 70~80 beats/min, and the optimal Lavi was 130 ms; heart rate >80 beats/min, and the optimal Lavi is 120 ms. It would be ideal if the pacemaker could dynamically adjust sav and PAV according to heart rate to obtain the optimal Lavi[9].

This study shows that the optimization of Lavi has a significant and long-term beneficial effect on the cardiac structure and function of patients with third degree atrioventricular block implanted with dual chamber pacemakers, and the effect on the function occurs immediately after the optimization. This is because after the optimization of Lavi, the mechanical coordination between left atrium and ventricle is immediately improved. Therefore, cardiac hemodynamic indexes such as EDT and IVRT of echocardiography can be rapidly improved. After the improvement of cardiac hemodynamics, the left atrial pressure will be reduced, and the long-term low left atrial pressure drop will effectively avoid the expansion of the left atrium. This is proved by the change of the left atrial volume index in the optimization group. The most obvious effect of optimizing Lavi is the improvement of LVEF, which indicates that improving the mechanical coordination of left atrium and ventricle is helpful to improve the overall systolic function of left ventricle[2].

Left atrial pressure, size and tissue characteristics are important factors affecting the occurrence of atrial fibrillation. This study found that after the optimization of Lavi, with the improvement of left ventricular filling and the reduction of left atrial volume, the incidence of atrial fibrillation decreased significantly, indicating that it is very necessary to further optimize Lavi after the implantation of dual chamber pacemakers in patients with third degree atrioventricular block, which can not only improve the mechanical function of the heart, but also effectively improve the electrical function. Because the observation time of this study is short, and the risk of clinical heart failure and death of patients in the optimization group and non optimization group is low, there is no difference in the observation of these index endpoints.

In conclusion, the results of this study show that optimized Lavi can improve the short-term hemodynamic effect and reduce or delay the occurrence of atrial fibrillation in patients with third degree atrioventricular block implanted with dual chamber pacemakers.

Conflict of interest

The authors declare no conflict of interest.

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