Original Article Use of a dual-chamber pacemaker to achieve an excellent response to cardiac resynchronization therapy in patients with dilated cardiomyopathy and complete left bundle branch block: a case report

Lijin Pu^{1,2*}, Yu Wang^{1,2*}, Lulu Zhao², Baotong Hua¹, Shumin Li¹, Ling Zhao^{1,2}, Tao Guo^{1,2}

¹Department of Cardiology, ²Institute of Cardiovascular Diseases, The First Affiliated Hospital of Kunming Medical University, Kunming, P. R. China. *Co-first authors.

Received June 14, 2016; Accepted August 15, 2016; Epub April 15, 2017; Published April 30, 2017

Abstract: The atrioventricular delay (AVD) in cardiac resynchronization therapy (CRT) is usually programmed to be shorter than the physiological AVD, which can lead to patients non-responsive to CRT. Although the programming of rate-adaptive AV delay (RAAVD) has been recommended for the optimization of the AVD in CRT with a triloculare pacemaker, the response to CRT is disappointing. Moreover, few studies have reported a dual chamber pacemaker to achieve response to CRT based on RAAVD algorithm. This study reported a 58-year-old male patient who was diagnosed with dilated cardiomyopathy and complete left bundle branch block. He achieved an excellent response to CRT with a dual-chamber pacemaker by left univentricular pacing with RAAVD algorithm.

Keywords: Cardiac resynchronization therapy, dilated cardiomyopathy, rate-adaptive atrioventricular delay algorithm, optimal atrioventricular delay

Introduction

Cardiac resynchronization therapy (CRT) has been demonstrated to significantly improve cardiac function and clinical outcomes in patients with New York Heart Association (NYHA) class III or IV congestive heart failure (CHF) and a left ventricular ejection fraction (LVEF) less than 30%. However, approximately 20-30% of patients are non-responsive to CRT [1]. Fixed short atrioventricular delay (AVD) in current CRT [2] has been considered as one of the reasons, which can abolish the physiological AVD of atrioventricular node (AVN), thereby counteracting the benefit of standard biventricular (BiV) pacing. It is well known that physiological AVD plays a key role in achieving optimal atrioventricular (AV) synchrony and atrial contribution to ventricular filling [3]. Therefore, the optimal AVD is important for patients' response to CRT. Currently, the programming of rate-adaptive AV delay (RAAVD) has been recommended for the optimization of the AVD in atrioventricular block pacing [4]. To date, few studies have reported a dual chamber (DDD) pacemaker achieving response to CRT based on RAAVD algorithm. Here, we reported a patient with dilated cardiomyopathy (DCM) and chronic complete left bundle branch block (CLBBB) who was implanted with a DDD pacemaker to achieve an excellent response to CRT by left-univentricular (LUV) pacing with a novel RAAVD algorithm.

Case presentation

A 58-year-old male patient was admitted to the hospital with palpitations and dyspnea after physical activities for more than 1 year (approved by ethical committee of the First affiliated hospital of Kunming medical university). There were no special records in the medical history and neither alcohol nor smoking addiction was recorded. Physical examination showed that cardiac dullness area was extended in the left side and no pathological murmurs were heard in all cardiac auscultation areas. Heart rate (HR) was 64 beats/min without arrhythmia



Figure 1. Comparation of QRS complex between before and after RAAV LUV pacing. A: Before CRT (CLBBB, QRS duration was 200 ms under intrinsic atrioventricular conduction). B: After LUV pacing with RAAV (QRS duration was 137 ms).

and LVEF was 34%. Electrocardiograph (ECG) revealed a sinus rhythm and CLBBB. Finally, the patient was diagnosed with DCM, CLBBB and NYHA class III by echocardiography.

Based on the diagnosis of DCM and CLBBB, the patient accepted the pacemaker implantation. After the informed consent to implantation of pacemaker was obtained, a DDD pacemaker (Relia RED01, Medtronic, Inc., Minneapolis, MN, USA) was implanted on October 15, 2013. The surgery of DDD pacemaker implantation was performed according to the standard procedure. X-ray percutaneous transluminal coronary angioplasty (PTCA) wire guided electrode of left ventricular lead to position in the left posterolateral cardiac vein and right atrium electrode in the right atrial appendage. The left ventricular electrode lead and right atrial electrode lead were connected to the jacks on the pulse generator correspondently. The operation was finished successfully without complications.

The patient was followed up after short time of interval optimization with echocardiography. Start and stop rates were set at 60 bpm and 100 bpm according to the lower and upper limit heart rate in holter ECG recording, respectively. Interval from onset of A wave to atrial sensing in intracardiac electrograms was 28 ms. Therefore, atrial sense compensation (ASC) was set at 30 ms, and PR interval at optimized ASC (190 ms - 30 ms) was taken as baseline interval (160 ms). Because a sensed AV (SAV) interval of 150 ms (160 ms -10 ms) achieved the largest aortic velocity-time integral (AVI), the optimal AVD was set at 150 ms. Then, RAAVD was programmed as following: SAV interval for start rate

= optimal AVD + (intrinsic PR interval at start rate - intrinsic PR interval at optimization) = 150 + (220 - 190) = 180 (ms); paced AV (PAV) interval for start rate = SAV interval for start rate + ASC = 180 + 30 = 210 (ms); and maximum offset was set at -40 ms (intrinsic PR interval at stop rate - intrinsic PR interval at start rate). Medications were unchanged during follow-up (oral administration of 40 mg furosemide and 25 mg spironolactone daily). Transthoracic echocardiogram was performed at the follow-up of 6 and 12 months after the device implantation. Cardiac output was assessed using the LV outflow tract velocity-

Table 1. NYHA class and echocardiographic
parameters of baseline, 6 and 12 months
post-implantation

	Before CRT	6 months post	12 months post
NYHA class	III	II	I
LVEF (%)	34	47	58
LVEDD (mm)	69	58	53
LAD (mm)	36	24	27
AVI (cm)	24.9	25.3	28.2
IVMD (ms)	111	74	69
E/A Pd (ms)	383	300	235
Ts-SD12 (ms)	92	61	70

NYHA, New York heart association; CRT, cardiac resynchronization therapy; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic diameter; LAD, left anterior descending; AVI, aortic velocity-time integral; IVMD, interventricular mechanical delay; E/A Pd, E/A procedure duration; Ts-SD12, standard deviation of time intervals of the 12 LV segments.

time integrals from apical five-chamber views. The cardiac function corresponding to each AVD was calculated after the AVD titrated for 5 min. Standard deviation of time intervals of the 12 LV segments (Ts-SD12) was measured.

During follow-up, the cardiac function of patient was found to recover very well. Therefore, the patient has never been admitted to hospital again. QRS duration was narrowed from 200 ms to 137 ms after LUV pacing with RAAVD (Figure 1). Compared with the baseline, echocardiographic parameters such as LVEF, left ventricular end-diastolic diameter (LVDD), Ts-SD12, AVI, interventricular mechanical delay time (IVMD), and E/A procedure duration (E/A Pd) were improved at 6 and 12 months postimplantation (Table 1). After DDD pacemaker implantation for 12 months, LVEF increased by 24%, and the patient remained in good condition without hospitalization. Chest X-ray showed that the cardiothoracic ratio (CTR) decreased from 56% to 49% (Figure 2). LVDD decreased from 68 to 53 (mm) and cardiac function improved from NYHA class III to I within 1 year. Ts-SD12 at base and papillary levels were improved from 92 ms to 70 ms (Figure 3). QRS duration and morphology did not change with varying HR. Threshold of pacing and sensing of LV lead were 0.75 V and 6 mV, respectively. Percentage of ventricular pacing was 99.7%. Left ventricular output was set at 2.0 V. The average battery life which was automatically calculated by the system was 10 years.

Discussion

In this study, for the first time, we implanted a dual chamber pacemaker and developed a novel algorithm to preserve the physiological AVD. The results showed that QRS duration was shortened after LUV pacing with RAAVD, as well as the echocardiographic parameters such as NYHA class, LVEF, LVDD, Ts-SD12, AVI, IVMD, and E/A Pd were all improved after DDD pacemaker implantation for 6 and 12 months, which suggested that the patient with DCM and CLBBB achieved an excellent response to CRT by LUV pacing with this novel RAAVD algorithm.

Our results showed that the LUV pacing with RAAVD algorithm shortened the QRS duration from 200 ms to 137 ms in patients with DCM and CLBBB. Because the BiV pacing activation was slowly conducted retrograde through cardiomyocytes via His-Purkinje system, the time for RV activation was longer under the standard BiV pacing than that for physiological activation, which manifested as the longer QRS duration. Previous research had proved that the abnormality of intraventricular conduction was associated with the extension of QRS duration, which increased the percentage of mechanical dyssynchrony, thereby leading to the lower cardiac function and the higher mortality [5]. Therefore, narrow QRS wave under LUV pacing with RAAVD algorithm may obtain more benefit than standard BiV pacing and LUV pacing with fixed AVD.

The first study of the RAAVD in patients with CRT was reported by Scharf et al. and the results showed that the optimal AVD increased during exercise and a progressive fusion at longer AVD might increase ventricular resynchronization [6]. Therefore, the recommendation by Scharf et al. was suggested to be used with extreme caution. In addition, determined the optimal AVD by simultaneous measurement of electrocardiographic and doppler-echocardiographic parameters, and then programmed the RAAVD in CRT [1]. The results showed that optimal AVD was shortened with increased HR and the RAAVD parameters in CRT patients was advised to be turned off. Excitingly, our study showed that QRS duration and morphology did not change with varying HR, which demonstrated that RAAVD algorithm could track physiological AVD and enable fusion of intrinsic right bundle conduction with paced LV conduction,



Figure 2. Chest X-ray before and 1 year after PM implantation. A: Before PM implantation, chest X-ray showed LV dilated. CTR was 56%. B: 12 months after PM implantation, great reduction in ventricular size, the CTR decreased from 56 to 49%.

thereby solving the problem that the changes of fusion and QRS duration resulted from fixed AVD and intrinsic conduction. This may partly explain the results of the previous studies which showed that fusion was not established and LV pacing was not superior to BiV pacing [7, 8]. Furthermore, the left-sided AVD automatically tracked physiological AVD by RAAV algorithm to allow fusion with intrinsic conduction coming from the normal-conducting right bundle branch, which averted the deleterious effects from right ventricular (RV) pacing, then increased device longevity due to unnecessary RV pacing. Higher percentage of ventricular pacing in patients with intact AVD had been found to be associated with increased incidence of atrial fibrillation and heart failure [9]. Our previous study showed that preserving intrinsic conduction via the right bundle branch potentially and pacing LV simultaneously could improve acute hemodynamic effect than standard right BiV pacing and avert deleterious effects from RV pacing [10].

AV and interventricular interval optimization were time-consuming in conventional BiV pacing, and it was difficult to achieve individualization and dynamic optimization [11]. However, under LUV pacing with RAAVD algorithm, the intrinsic PR interval was the physiological and optimal AVD, it was unnecessary to optimize. Therefore, LUV pacing RAAVD algorithm could realize dynamic optimization of AVD, which adapted to physiological alterations during exercise and sympathetic tone changes, and thereby preserving optimal atrial contribution to ventricular filling. However, a randomized, multicenter, double-blind, controlled clinical research is needed to confirm our finding.

The algorithm tracking physiological AVD in LUV pacing will contribute to the research and development of new pacemaker. Previous study had shown that the numerous proposed methods, including predefined formulas, iterative methods and automatic methods, were used to obtain optimized AVD. Recent study had shown that adaptive CRT algorithm (Medtronic, Inc.) significantly reduces RV pacing and improves response rates to CRT [12]; however, adaptive CRT algorithm was based on three chamber pacemaker.

In conclusion, our LUV pacing with RAAVD algorithm could be used in both dual and threechamber pacemaker. This novel algorithm will cause dispute on preserve or abolish of the physiological AVD of AVN in CRT. The patient with DCM and CLBBB who use dual-chamber pacemaker achieved superior response to CRT by LUV pacing with RAAVD algorithm.



Figure 3. Ts-SD12 at base and papillary level were also improved 12 months after RAAV LUV pacing. A: TS-SD12 was 92 ms before RAAV LUV pacing; B: TS-SD12 was 70 ms 12 months post-implantation.

Acknowledgements

This study was supported by two grants from National Natural Science Foundation of China National Science Foundation (81360044) and Yunnan Science and Technology Committee (2013FB133).

Disclosure of conflict of interest

None.

Address correspondence to: Drs. Ling Zhao and Tao Guo, Department of Cardiology, The First Affiliated Hospital of Kunming Medical University, 295 Xi Chang Road, Kunming 650032, P. R. China. Tel: +8687165324888; Fax: +8687165377618; E-mail: zhaolin580@126.com (LZ); guotao20@hotmail.com (TG)

References

- [1] Melzer C, Bondke H, Körber T, Nienaber CA, Baumann G and Ismer B. Should we use the rate-adaptive AV delay in cardiac resynchronization therapy-pacing? Europace 2008; 10: 53-58.
- [2] Ellenbogen KA, Gold MR, Meyer TE, Lozano IF, Mittal S, Waggoner AD, Lemke B, Singh JP, Spinale FG and Van Eyk JE. Primary Results From the SmartDelay Determined AV Optimization: A Comparison to Other AV Delay Methods Used in Cardiac Resynchronization Therapy (SMART-AV) Trial A Randomized Trial Comparing Empirical, Echocardiography-Guided, and Algorithmic Atrioventricular Delay Programming in Cardiac Resynchronization Therapy. Circulation 2010; 122: 2660-2668.
- [3] Antonini L, Auriti A, Pasceri V, Meo A, Pristipino C, Varveri A, Greco S and Santini M. Optimization of the atrioventricular delay in sequential and biventricular pacing: physiological bases, critical review, and new purposes. Europace 2012; 14: 929-938.
- [4] Melzer C, Körber T, Theres H, Nienaber CA, Baumann G and Ismer B. How can the rateadaptive atrioventricular delay be programmed in atrioventricular block pacing? Europace 2007; 9: 319-324.
- [5] Iuliano S, Fisher SG, Karasik PE, Fletcher RD and Singh SN. QRS duration and mortality in patients with congestive heart failure. Am Heart J 2002; 143: 1085-1091.

- [6] Scharf C, Li P, Muntwyler J, Chugh A, Oral H, Pelosi F, Morady F and Armstrong WF. Ratedependent AV delay optimization in cardiac resynchronization therapy. Pacing Clin Electrophysiol 2005; 28: 279-284.
- [7] Rao RK, Kumar UN, Schafer J, Viloria E, De Lurgio D and Foster E. Reduced ventricular volumes and improved systolic function with cardiac resynchronization therapy a randomized trial comparing simultaneous biventricular pacing, sequential biventricular pacing, and left ventricular pacing. Circulation 2007; 115: 2136-2144.
- [8] Thibault B, Ducharme A, Harel F, White M, O'Meara E, Guertin MC, Lavoie J, Frasure-Smith N, Dubuc M and Guerra P. Left ventricular versus simultaneous biventricular pacing in patients with heart failure and a QRS complex ≥ 120 milliseconds. Circulation 2011; 124: 2874-2881.
- [9] Sweeney MO, Hellkamp AS, Ellenbogen KA, Greenspon AJ, Freedman RA, Lee KL and Lamas GA. Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation 2003; 107: 2932-2937.
- [10] Pu LJ, Wang Y, Zhao L, Luo ZL, Hua BT, Han MH, Li SM, Yang J, Li L, Peng YZ and Guo T. Cardiac resynchronization therapy (CRT) with right ventricular sense triggered left ventricular pacing benefits for the hemodynamics compared with standard CRT for chronic congestive heart failure: A cross-over study. Cardiol J 2015; 22: 80-86.
- [11] Brugada J, Brachmann J, Delnoy PP, Padeletti L, Reynolds D, Ritter P, Borri-Brunetto A and Singh JP. Automatic Optimization of Cardiac Resynchronization Therapy Using SonR-Rationale and Design of the Clinical Trial of the SonRtip Lead and Automatic AV-VV Optimization Algorithm in the Paradym RF SonR CRT-D (RESPOND CRT) Trial. Am Heart J 2014; 167: 429-436.
- [12] Singh JP, Abraham WT, Chung ES, Rogers T, Sambelashvili A, Coles JA and Martin DO. Clinical response with adaptive CRT algorithm compared with CRT with echocardiography-optimized atrioventricular delay: a retrospective analysis of multicentre trials. Europace 2013; 15: 1622-1628.