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Original Article

Evaluation of cardiac function by pacing at different right ventricular sites in patients with third-degree atrioventricular block using Doppler ultrasound

Qing Zhao, Jin-Shan Wo, Jie Guo, Shang-Lang Cai

Departments of Cardiology, Affiliated Hospital of Qingdao University Medical College, Qingdao 266003, China

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Abstract: *Objective*: This study utilized Doppler ultrasonography cardiograms in patients with third-degree atrioventricular (III-AV) block to compare right ventricular apex (RVA) pacing and right ventricular outflow tract (RVOT) pacing with respect to their effects on synchronization of contraction between the two ventricles, as well as on timing of specific left-ventricular electrical and mechanical events and their impact on left ventricular function. *Methods:* Thirty-eight patients with (III-AV) block were implanted with dual-chamber pacemakers, in 20 cases, implantation occurring in the RVOT (RVOT group), while in 18 cases implantation occurred in the RVA (RVA group). Patients underwent Doppler echocardiography and electrocardiography (ECG) one month pre- and one month post-surgery, as well as 12 months post-surgical implantation of the pacemaker. *Results*: Prior to pacemaker implantation, no significant differences were found between the two groups with respect to the following parameters: left ventricular end-diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), left ventricular ejection fraction (LVEF), E/A value (ratio of early [E] to late [A] ventricular filling velocities), inter-ventricular mechanical delay (IVMD) and septal-to-posterior wall motion delay (SPWMD). One month after implantation, no significant differences were found between the two groups for LVEDD, LVESD, LVEF, and E/A. However, compared with the RVOT group, the RVA group exhibited prolonged IVMD and SPWMD. Twelve months after pacemaker implantation, there was no significant difference for E/A between the two groups; however, compared with the ROVT group, the RVA group exhibited prolonged LVEDD, LVESD, IVMD, and SPWMD and significantly lower LVEF. Conclusion: Relative to RVA pacing, RVOT pacing mitigated impairment of systolic function and systolic dys-synchronization.

Keywords: Third-degree atrioventricular block, Doppler echocardiography, pacemakers, right ventricular outflow tract, interventricular mechanical delay septal-to-posterior wall motion delay

Introduction

Because of the ease of implanted electrode fixation, a low rate of dislocation, and a steady threshold value, right ventricular apex (RVA) pacing has traditionally been the major clinical ventricular pacing site of choice. However, RVA pacing produces an abnormal direction of ventricular depolarization, with an asynchronous mechanical motion, resulting in both systolic and diastolic dysfunction and ventricular remodeling [1-3]. Various experimental and clinical studies have shown that right ventricular apex pacing will cause abnormal sequences of both cardiac depolarization and mechanical motion, thereby leading to an increase in cardiovascular disease morbidity and mortality [4-6]. For patients with third-degree atrioventricular (III-AV) block who require ventricular pacing, the search for pacing sites other than the cardiac apex has become a quite active research area.

With respect to active-electrode placement, right ventricular outflow tract pacing (RVOT) has generated considerable interest given that its characteristics are closer to the physiological sequence of ventricular activation during a normal cardiac cycle [7]. RVOT pacing shows similar outcomes to a His bundle electrogram (HBE), with pacemaker current capable of normally passing through the ventricular conduction system and rapidly activating the left and right ventricles; consequently, this provides the poten-

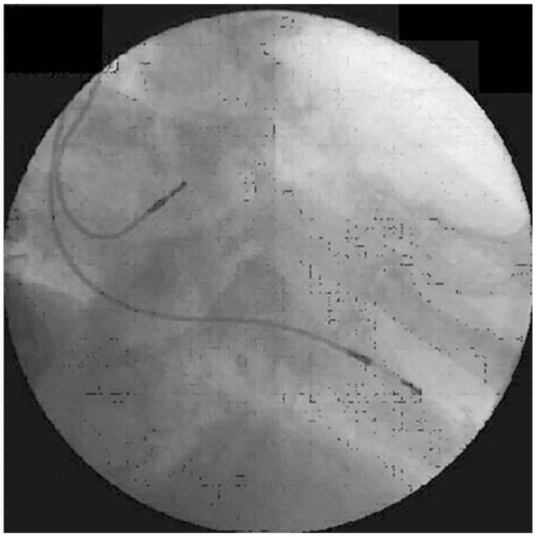

Figure 1. X-ray of electrodes fixed on the right auricle and ventricular apex (RVA).

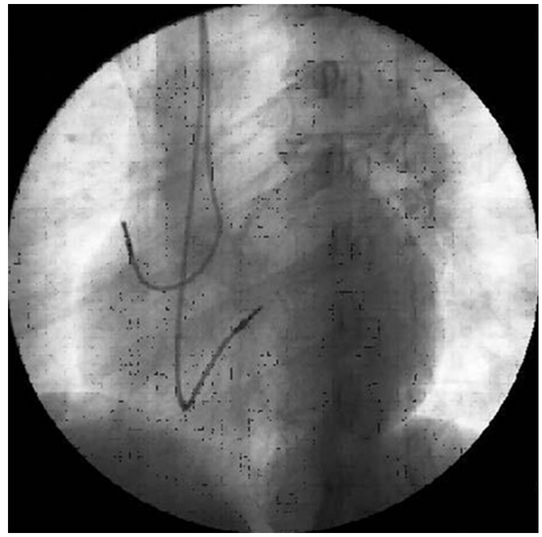

Figure 2. X-ray of electrodes fixed on the right auricle and ventricular output tract (RVOT). Positioning criteria: under the projection of the left anterior oblique at 45°, the electrode tip pointed toward the rear of the right ventricular outflow tract.

tial advantage of improving the synchronization of inter-ventricular and intra-ventricular electrical and mechanical activities. Previous research has demonstrated RVOT electrode performance and stability of pacing parameters [8]. The current research utilized Doppler ultrasonography to evaluate and contrast the therapeutic effectiveness of pacemaker implantation at different right ventricular sites in the treatment of patients with (III-AV) block.

Previous studies have shown that, for patients with normal cardiac function immediately after pacemaker implantation, the cardiac function of RVA and RVOT groups was somewhat impacted, but there was no significant difference between the two groups [9, 10]. In other studies, patients with high-degree atrioventricular block and normal cardiac function 7 or 8 years after RVA pacemaker implantation, 26% had succumbed to heart failure, which largely occurred within three years after implantation. In contrast, RVOT pacing with accurate positioning and long-term follow-up confirmed that RVOT could preserve left ventricular function to a certain extent [11-13].

Materials and methods

Methods

Thirty-eight III-AV block patients treated with implanted dual-chamber pacemakers and hospitalized from April 2009 to October 2010 in the department of cardiology of the Affiliated Hospital of Qingdao University were selected for this clinical study. We used dual pacing, dual sensing, dual response (DDDR) pacemaker obtained from either Medtronic (Medtronic, Inc., Minneapolis, MN, USA) or St. Jude (St. Jude Medical, Inc., Saint Paul, Minnesota, USA). In 20 patients, electrodes were implanted in the right ventricular outflow tract (RVOT group, n = 20), while 18 patients had electrodes implanted in the right ventricular apex (RVA group, n = 18). Patients with the following conditions were excluded from the study: Grade IV heart function (NYHA classification), left ventricular ejection fraction (LVEF) ≤ 40%, valvular heart disease, cardiomyopathy, coronary heart disease, arrhythmia, and patients already implanted with a permanent cardiac pacemaker. In order to ensure equivalent proportions of ventricular pacing in the two groups, patients with III-AV block were randomly assigned to RVA or RVOT. Subsequent to patient selection, both one-month and 12-month ultrasonographic follow-ups were performed to compare relevant parameters between RVOT and RVA groups, in terms of benefits to cardiac function.

The study protocol was approved by the Institutional Review Committee on Human Research of The Affiliated Hospital of Qingdao University, and informed consent was ob-

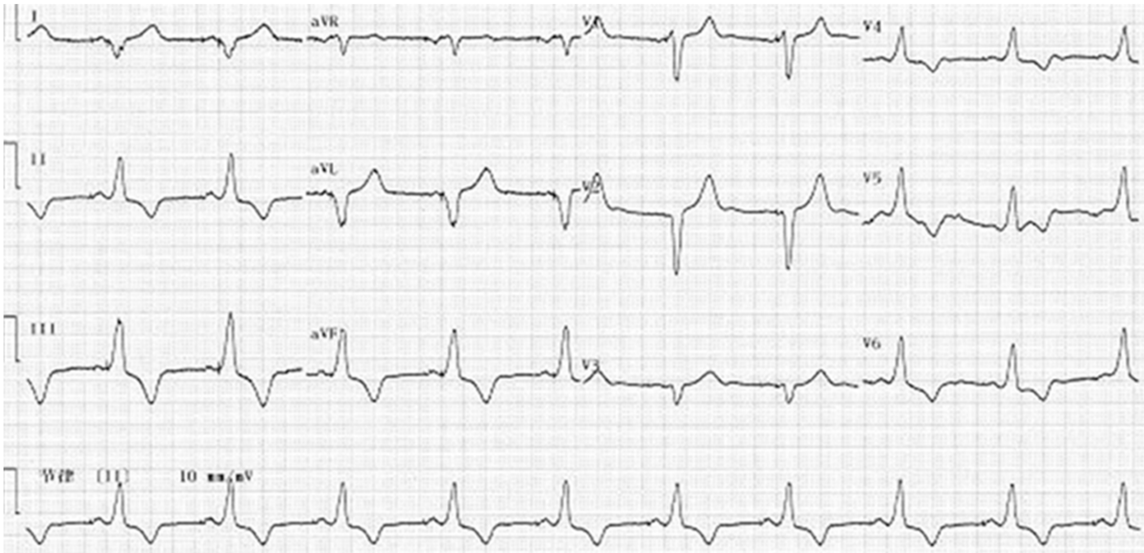

Figure 3. ECG: for leads II, III and avF, the dominant wave points upward, while for lead avR, the dominant wave points downward. Lead I shows QS-type, rs-type, or R-type patterns. This is designated as RVOT pacing.

tained from all study subjects prior to their participation.

Selection and implantation of pacemakers

DDDR pacemakers from either Medtronicor St.Jude were utilized. With respect to wire leads, CapSure Sense 4074 passive wire (Medtronic) or 1642T passive wire (St.Jude) were used for atrium; for ventricle, either CapSureFix Novus 5076 fixed wire (Medtronic), CapSure Sense 4074 passive fixed wire (Medtronic), Tendril SDX 1888T active wire (St. Jude), or 1646T passive wire (St. Jude) were employed. The Philips SONOS5500 cardiac color Doppler ultrasonic diagnostic apparatus (Philips N.V., Amsterdam, Netherlands) was utilized for ultrasonography. This instrument was equipped with S3 and S4 ultra-wideband phased array electronic probes, with probe frequency of 1.0~4.0 MHz and a simultaneously recording electrocardiogram.

A trial electrodes were fixed on the right auricle and ventricular electrodes were fixed on either the RVA (**Figure 1**) or RVOT (**Figure 2**). Positioning criteria of RVOT interval pacing was as follows: under the projection of the left anterior oblique, at 45°, the electrode tip pointed toward the rear (posteriorly, toward the spine) of the right ventricular outflow tract. The pacing ECG showed that for leadsII, III and avF, the dominant wave pointed upward, while for lead avR, the dominant wave pointed downward. Lead I showed QS-type, rs-type, or R-type patterns. This was designated as RVOT pacing (**Figure 3**). The lead V1~V6 QRS wave complex provided a graphical block of the left bundle branch and was designated as septal (RVA) pacing (**Figure 4**) [14].

Measurement and follow up of the Doppler ultrasonic cardiogram

Immediately post-surgery, the atrioventricular delay (AVD) was found to be in the range of 127 ± 33 ms, during this time period, and considering both systolic and diastolic function, the myocardial performance index (MPI) was at a minimum [15]. This would reduce the impact of AV de-synchronization on cardiac function.

We measured and compared cardiac function and cardiac motion synchronization indicators for both RVA and RVOT groups, one month preoperatively, and both one and 12 months postoperatively. Indicators reflecting left ventricular function were the following: left ventricular end-diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), left ventricular ejection fraction (LVEF), E/A value, the velocity time integral (VTI) of the aortic valve orifice, and mitral valve regurgitation flow.

Indicators reflecting synchronization of cardiac motion were the following: interventricular

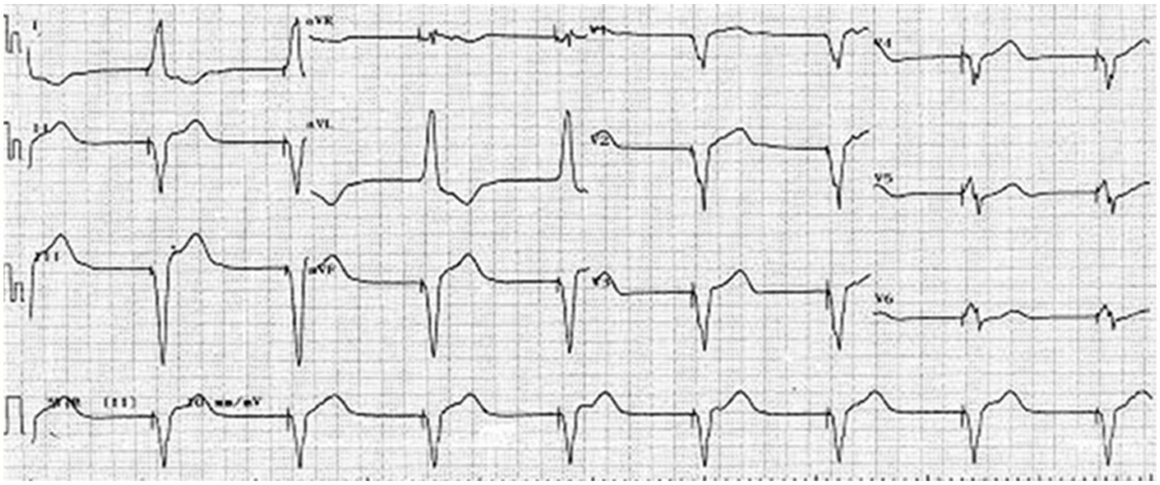

Figure 4. ECG: The lead V1~V6 QRS wave complex provides a graphical block of the left bundle branch and is designated as septal (RVA) pacing.

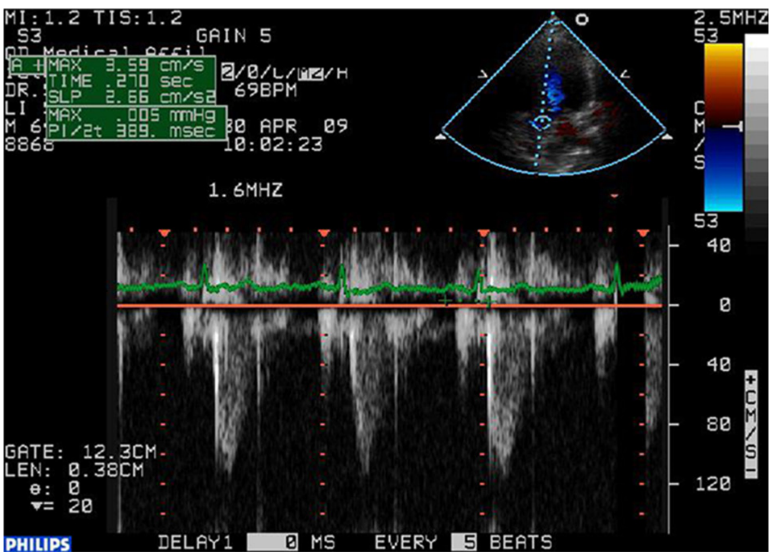

Figure 5. Doppler echo-cardiography: left ventricular ejection time.

mechanical delay (IVMD), and septal-to-posterior wall motion delay (SPWMD). IVMD represents the difference in pre-ejection time between the left and right ventricles. Under normal circumstances, left ventricular ejection time is slightly longer than that of the right ventricle, but the difference is normally less than 30 ms. Under conditions of either left bundle branch block or right ventricular pacing, mechanical activity of the left and right ventricles will lose synchronization, and the value of the difference in pre-ejection time of the left and right ventricles will increase. To ascertain the pre-ejection time of the right ventricle, the time interval from the beginning of the QRS wave group to the initial pulmonary artery blood flow is measured over three continuous cardiac cycles and averaged. The same method is used to measure pre-ejection time of the left ventricle, using the initiation of blood flow through the aortic valve. Subtracting pulmonary artery pre-ejection interval (PPEI) and aortic pre-ejection interval (APEI) gives the value of the difference in pre-ejection time between the left and right ventricles; if that value is greater than 40 ms, a diagnosis rendered of de-synchronization of systolic activity in left (**Figure 5**) and right (**Figure 6**) ventricles [16-18]. For SPWMD, measuring left ventricular dys-synchrony, parasternal long-axis M-mode echo-cardiography and the moving curve of the left ventricular back wall is utilized. The time duration is measured from the peak of ventricular septum contraction to the peak of left ventricular posterior wall contraction; this yields, SPWMD, which, under normal circumstances, it is no greater than 130 ms (**Figure 7**).

Statistical analysis

Statistical analysis was performed with SPSS software, version 13.0 (SPSS Inc., Chicago, IL,

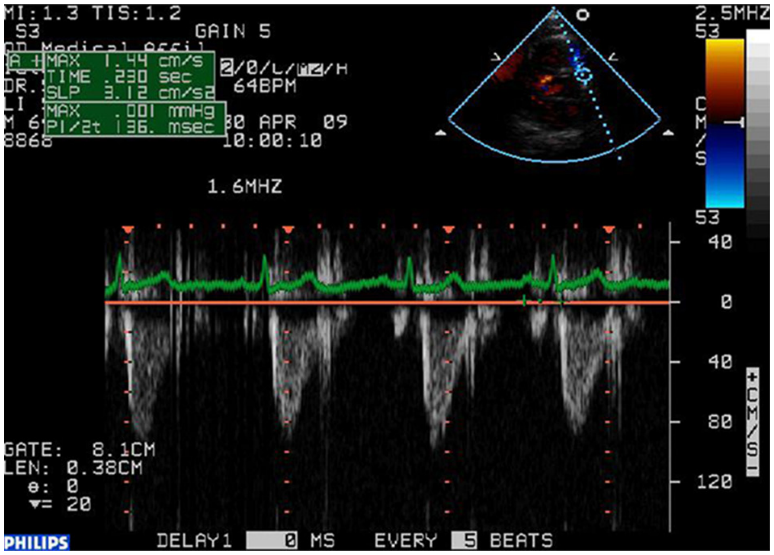

Figure 6. Doppler echocardiography: right ventricular ejection time.

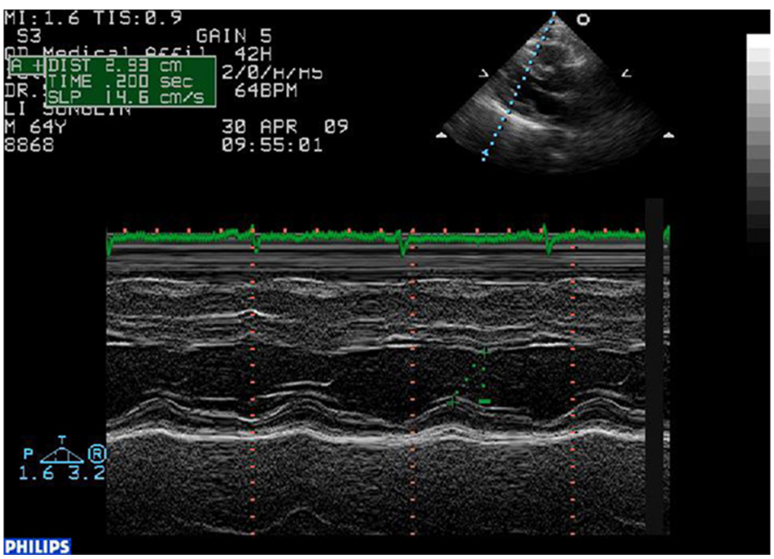

Figure 7. M-mode echocardiography measuring septal-to-posterior wall motion delay (SPWMD)-the duration from peak ventricular septum contraction to the peak of left ventricular posterior wall contraction.

USA). Measurement data was expressed as mean ± standard deviation; t test was used for mean comparison between the two samples. Statistical significance was defined as $P < 0.05$.

Results

Surgery was successfully completed for all 38 cases, 18 RVA and 20 RVOT pacing. A follow up analysis showed no electrode dislocation, displacement, pouch infections, or other complicating diseases, and pacing function was good.

Doppler ultrasonic cardiography was utilized to measure the impact of the two different pacing methods on cardiac function. Results showed that prior to pacemaker implantation, no statistically significant difference was found between the RVA and RVOT groups for LVEDD, LVESD, LVEF, and E/A. This was likewise the case for the analysis of these parameters one month after pacemaker implantation. However, a follow-up analysis one year after surgery showed the following (**Table 1**): while no significant difference was found for the E/A value, the LVEDD of the RVA pacing group was larger than that of the RVOT pacing group (49.11 ± 2.39 mm vs. 47.4 ± 1.96 mm, P = 0.02). In addition, the LVESD was also larger for the RVA group (34.28 ± 3.41 mm vs. 32.5 ± 1.5 mm, P = 0.04), while the LVEF was decreased for RVA compared with that of RVOT (0.59 ± 0.04 vs. 0.62 ± 0.03, P = 0.02). These findings indicate that compared with RVOT pacing, RVA pacing was more likely to impair left ventricular function.

Doppler ultrasonic cardiography was also used to measure the impact of the two different pacing methods on desynchronization of ventricular movements (**Table 2**). Results showed that prior to pacemaker implantation, there was no significant difference between the two groups for IVMD and SPWMD. However, one month after implantation, the two groups demonstrated obvious differences. Compared with the RVOT pacing group, both the IVMD and SPWMD of the RVA pacing group were significantly longer; for IVMD, 39.83 ± 6.09 ms, RVA vs. 31.95 ± 7.86 ms, RVOT (P = 0.02); for SPWMD, 97.83 ± 20.81 ms, RVA vs. 84.6 ± 10.89 ms, RVOT (P = 0.023). Twelve months after pacemaker implantation, the IVMD, and SPWMD of both groups became

Table 1. Standard Doppler echocardiographic quantitative analysis ($\overline{x}$ ± s)

	RVA group	RVOT group	*P*
Before implantation			
LVEDD (mm)	46.11 ± 1.64	46.55 ± 2.06	0.476
LVESD (mm)	29.28 ± 3.33	29.10 ± 1.51	0.83
E/A	0.93 ± 0.04	0.94 ± 0.03	0.1
LVEF (%)	67.22 ± 2.12	67.0 ± 1.62	0.71
1 M post-implantation			
LVEDD (mm)	46.39 ± 1.37	46.9 ± 1.97	0.36
LVESD (mm)	30.2 ± 1.39	29.85 ± 1.42	0.42
E/A	0.94 ± 0.027	0.96 ± 0.024	0.12
LVEF (%)	64.22 ± 5.33	66.1 ± 3.12	0.207
12 M post-implantation			
LVEDD (mm)	49.11 ± 2.39	47.40 ± 1.96	0.021
LVESD (mm)	34.28 ± 3.41	32.5 ± 1.50	0.041
E/A	0.91 ± 0.23	0.96 ± 0.02	0.23
LVEF (%)	59.56 ± 3.38	62.80 ± 2.14	0.001

Statistical significance was defined as $P < 0.05$.

Table 2. Doppler ultrasonic cardiogram measurements of the impact of the twodifferent pacing methods on de-synchronization of ventricular movements ($\overline{x}$ ± s)

	RVA group	RVOT group	*P*
Before implantation			
IVMD (mm)	8.23 ± 0.76	8.63 ± 0.74	0.113
SPWMD (mm)	43.38 ± 11.93	42.6 ± 8.12	0.722
1 M post-implantation			
IVMD (mm)	39.83 ± 6.01	31.95 ± 7.86	0.002
SPWMD (mm)	97.83 ± 20.81	84.6 ± 10.89	0.023
12 M post-implantation			
IVMD (mm)	48.83 ± 8.42	41.5 ± 11.01	0.028
SPWMD (mm)	143.89 ± 12.43	136.45 ± 8.37	0.03

Statistical significance was defined as $P < 0.05$.

larger and there were significant differences between them. IVMD for RVA was 48.83 ± 8.42 ms, while for RVOT, it was41.5 ± 11.01 ms (P = 0.02); for SPWMD, RVA was 143.89 ± 12.43 ms, while for RVOT, it was 136.45 ± 8.37 (P = 0.03) (**Table 2**). These findings indicate that compared with RVOT pacing, RVA pacing was more likely to cause de-synchronization of ventricular movements.

Discussion

Over the course of this 30-month study, the pacing threshold of RVOT and RVA was confirmed, and consistent with prior studies, there was no significant difference in R wave sensing and pacing electrode impedance, indicating that RVOT pacing was safe and effective. However, our study showed that one year after pacemaker implantation, cardiac function was more negatively impacted by RVA pacing as compared with RVOT pacing.

Studies have shown that dual-chamber pacemakers enable a return to physiological heart rate in patients with third-degree atrioventricular block, while RVA pacing results in a loss of the normal ventricular activation sequence, causing de-synchronization of inter-ventricular and intra-left ventricular function at an early stage after surgery; however, long-term follow up studies have been rare. In the present study, Doppler ultrasonic cardiography was repeatedly utilized, both before and after surgery, to measure the difference in pre-ejection time of both left and right ventricles, as well as SPWMD, in order to evaluate the de-synchronization of both left ventricular and in ter-ventricular movements. Results showed that, compared with RVOT pacing, RVA pacing appeared to cause significant de-synchronization of inter-ventricular and left ventricular movements.

In summary, under the premise of conditions such as pacing mode, ventricular pacing proportion, and consistency of optimized atrioventricular conduction, the impacts of RVOT and RVA pacing on cardiac function and cardiac motion synchronization were compared in this study. Our preliminarily results reveal that compared with RVA pacing, RVOT pacing had a smaller adverse impact on cardiac function and cardiac motion synchronization. However, the number of patients in this study was small, and the follow-up time was limited, suggesting that longer-term research with larger patient populations should be conducted to further illustrate the differences between RVOT pacing and RVA pacing in restoring cardiac function in (III-AV) block patients.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Qing Zhao, Departments of Cardiology, Affiliated Hospital of Qingdao University Medical College, Qingdao 266003 China. Tel: +86-0532-82911307; Fax: +86-0532-82911307; E-mail: zhaoqig_zq@163.com

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