Original Article

Influence of the Right Ventricular Lead Location on Ventricular Arrhythmias in Cardiac Resynchronization Therapy

Hao Su[1], Pei Bao[2], Kang-Yu Chen[1], Ji Yan[1], Jian Xu[1], Fei Yu[1], Dong-Mei Yang[3]

[1]Department of Cardiology, Anhui Provincial Hospital Affiliated to Anhui Medical University, Hefei, Anhui 230000, China
[2]Department of Electrocardiogram, Anhui Institute of Cardiovascular Diseases, Hefei, Anhui 230000, China
[3]Department of Echocardiography, Anhui Provincial Hospital Affiliated to Anhui Medical University, Hefei, Anhui 230000, China

Hao Su and Pei Bao contributed equally to this paper.

Abstract

Background: The influence of different right ventricular lead locations on ventricular arrhythmias (VTA) in patients with a cardiac resynchronization therapy (CRT) is not clear. This study aimed to evaluate the influence on VTA in patients with a CRT when right ventricular lead was positioned at the right ventricular middle septum (RVMS) and the right ventricular apical (RVA).

Methods: A total of 352 patients implanted with a CRT-defibrillator (CRT-D) between May 2012 and July 2016 in the Department of Cardiology of Anhui Provincial Hospital were included. Two-year clinical and pacemaker follow-up data were collected to evaluate the influence of the right ventricular lead location on VTA. Patients were divided into the RVMS group ($n = 155$) and the RVA group ($n = 197$) based on the right ventricular lead position. The VTA were compared between these two groups using a Kaplan-Meier curve and Cox multivariate analysis.

Results: When the left ventricular lead location was not considered, RVMS and RVA locations did not affect VTA. However, the subgroup analysis results showed that when the left ventricular lead was positioned at the anterolateral cardiac vein (ALCV), the RVMS group had an increased risk of ventricular arrhythmias and appropriate defibrillation (hazard ratio [*HR*] = 3.29, $P = 0.01$ and *HR* = 4.33, $P < 0.01$, respectively); when the left ventricular lead was at the posterolateral cardiac vein (PLCV), these risks in the RVMS group decreased (*HR* = 0.45, $P = 0.02$ and *HR* = 0.33, $P < 0.01$, respectively), and when the left ventricular lead was at the lateral cardiac vein, there was no difference between the two groups. In regard to inappropriate defibrillation, there was no significant difference among all these groups.

Conclusions: When the left ventricular lead was positioned at ALCV or PLCV, the right ventricular lead location was associated with VTA and appropriate defibrillation after CRT. Greater distances between leads not only improved cardiac function but also may reduce the risk of VTA.

Key words: Cardiac Resynchronization Therapy; Heart Failure; Ventricular Remodeling; Ventricular Arrhythmias

Introduction

Cardiac resynchronization therapy (CRT) can significantly improve the cardiac function of chronic heart failure patients with cardiac asynchrony. In addition to reducing the hospitalization rate for heart failure and hard endpoints such as all-cause mortality,[1,2] CRT can also reduce the risk of ventricular arrhythmias (VTA).[3] A subgroup study in the MADIT-CRT showed that the number of VTA and appropriate defibrillation in patients with left ventricular ejection fraction (LVEF) >50% after CRT significantly decreased, whereas there was no significant change in patients with LVEF <35%.[4] The antiarrhythmic function of CRT may be associated with

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.243560

Address for correspondence: Prof. Jian Xu, Department of Cardiology, Anhui Provincial Hospital Affiliated with Anhui Medical University, Hefei, Anhui 230000, China
E-Mail: slyyxj11@126.com

Received: 20-07-2018 **Edited by:** Ning-Ning Wang
How to cite this article: Su H, Bao P, Chen KY, Yan J, Xu J, Yu F, Yang DM. Influence of the Right Ventricular Lead Location on Ventricular Arrhythmias in Cardiac Resynchronization Therapy. Chin Med J 2018;131:2402-9.

improvements in myocardial remodeling and electrical remodeling.[5-7]

Previous studies showed that the left ventricular lead location has an important influence on myocardial remodeling and arrhythmias in CRT patients. Compared with the apex and anterior wall, the lateral wall and posterior lateral wall have better responsiveness and confer a lower risk of VTA.[8,9] However, few studies have been reported on the influence of the right ventricular lead position, and the results are not consistent.[10-12] However, it has been shown that the right ventricular lead position affects myocardial remodeling corresponding to different left ventricular lead positions; in addition, the improvement in myocardial remodeling might be associated with the distance between left and right ventricular leads or electrical separation.[13,14] The CRT efficacy may increase for greater distances between the right ventricular lead position and the left ventricular lead position. However, the effect of lead distance on VTA remains unclear.

This study analyzed the clinical and implantable cardioverter defibrillator (ICD) follow-up data in patients with a CRT-defibrillator (CRT-D). We compared the influence of different right ventricular lead positions on VTA.

Methods

Ethical approval

This study was approved by the Ethics Committee of Anhui Provincial Hospital Affiliated to Anhui Medical University, Hefei, Anhui, China.

Study population

Patients implanted with a CRT-D between May 2012 and July 2016 in the Department of Cardiology of Anhui Provincial Hospital were enrolled. The inclusion criteria of patients were as follows: over the age of 18 years, having received optimal pharmacological treatment before implantation, a QRS duration ≥120 ms, a New York Heart Association (NYHA) class of II–IV, LVEF ≤35%, primary and secondary prevention, and having received at least 12 months of echocardiography follow-up and device follow-up. The exclusion criteria of patients were as follows: having received coronary artery bypass, a pacemaker upgrade, permanent atrial fibrillation, not receiving regular follow-ups, or incomplete data. Enrolled patients were divided into the right ventricular apical (RVA) group and the right ventricular middle septum (RVMS) group based on the right ventricular lead position.

Baseline information

General demographic and clinical data of patients were collected. Clinical data included NYHA classification, cardiomyopathy etiology, ICD prophylaxis indication, echocardiography, electrocardiography, antiarrhythmic drug, and imaging data of intraoperative left and right ventricular lead locations.

Localization of lead positions

The lead positions were localized according to the intraoperative imaging data. Right ventricular lead positioning was performed using the SPICE trail method.[15] According to the intraoperative fluoroscopic, when the lead was at the border of the right ventricle at the right anterior oblique view (RAO ≥15°) and the lead went down and pointed toward the spine at the left anterior oblique view (LAO ≥30°), it was defined as RVA. The RVMS was positioned such that the lead pointed toward the septum at the RAO view, the lead was between the right ventricular outflow tract and the lower edge of the tricuspid valve, and the lead pointed horizontally toward the spine or slightly upward at the LAO view and avoided pointing toward the left lateral position at the right ventricular free wall [Figure 1a].

The left ventricular lead position was localized based on LAO view and was divided into three equal regions as shown in Figure 1b: the anterolateral cardiac vein (ALCV), the lateral cardiac vein (LCV), and the posterolateral cardiac vein (PLCV). RAO view was performed to avoid implantation of the lead into the apical location.

Parameters including the sensing, impedance, and pacing threshold values of the left and right ventricular leads were measured after implantation. All imaging data of the left and right ventricular lead positions were acquired by an independent electrophysiology expert who was blinded to the grouping condition. The determination results that were not consistent with the initial implantation positions were excluded from this study.

Pacemaker program

All patients underwent routine postoperative follow-up 1, 3, and 6 months after CRT-D implantation and every 6 months thereafter. The 2-year follow-up data were analyzed. If a defibrillation event of the pacemaker occurred, timely follow-up was performed. The model of the CRT-D program was monitoring combined with treatment, and the primary prophylaxis parameters of the pacemaker program was according to previous studies.[16,17] A control program strategy was adopted to reduce inappropriate discharge, and there were two or three recognition intervals. In primary prophylaxis, the VTA recognition frequency was usually 170 times/min. The treatment measure was performed after 60 s of monitoring.

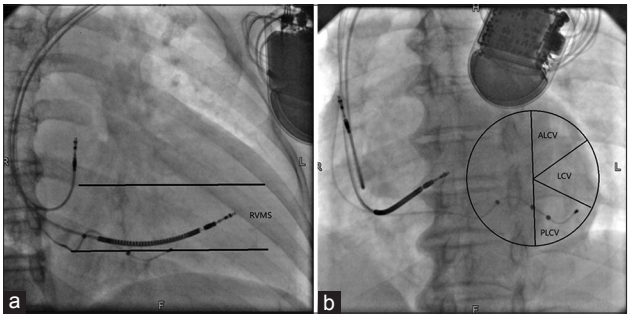

Figure 1: The lead positions were localized by fluoroscopic imaging. (a) RV lead positioned at the RVMS in the RAO 40° view; (b) LV lead position at PLCV in the LAO 30° view. RVMS: Right ventricular middle septum; ALCV: Anterolateral cardiac vein; LCV: Lateral cardiac vein; PLCV: Posterolateral cardiac vein; RAO: Right anterior oblique; LAO: Left anterior oblique; RV: Right ventricular; LV: Left ventricular.

When the fast ventricular arrhythmia frequency reached 200 times/min, antitachycardia pacing (ATP) was performed after 12 s of recognition. If ATP fails, a shock was used. When the ventricular fibrillation frequency was 250 times/min, during the initiation of ATP, a shock was directly performed after 2.5 s. The secondary prevention usually reduced the VTA recognition frequency of the pacemaker to 20 times/min based on the VTA frequency of the patient. The ventricular fibrillation frequency was the same as that in the primary prophylaxis. The pacemaker therapy was divided into appropriate defibrillation and inappropriate defibrillation.[18] Appropriate defibrillation was defined as VTA or ventricular defibrillation with a frequency difference within 40 ms. Inappropriate defibrillation was defined as atrial tachycardia or atrial fibrillation confirmed by electrocardiography with a frequency difference greater than 40 ms. All arrhythmia events and pacemaker treatment information were determined by professional pacemaker follow-up electrophysiology experts.

Echocardiography

Conventional cardiac echocardiography examinations were performed before implantation and 12 months after implantation. A Philips IE33 echocardiography diagnosis instrument (S5-1 probe; Philips, Eindhoven, The Netherlands) was used. The patient assumed a left lateral recumbent position, and the cardiac images of the four apical chambers were obtained. Three cardiac cycles were continuously measured. LVEF, left ventricular end-diastolic volume (LVEDV), and left ventricular end-systolic volume (LVESV) were obtained using Simpson's method; responsiveness was considered for LVEF improvement >10%.[19]

Statistical analysis

The statistical software used was SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were described using the mean ± standard deviation (SD), and categorical data were expressed as a percentage (%). Continuous variables with a normal distribution in the baseline data between groups were examined using the independent samples *t*-test. Percentages were compared using the Chi-square test. Ranked data were examined using a Wilcoxon Mann-Whitney test. The Kaplan-Meier curve and Cox multivariate regression analysis were used to evaluate the influence of the right ventricular lead position on VTA events and appropriate defibrillation, with comparisons of cumulative event rates by using the log-rank test. Gender, ischemic cardiomyopathy, primary prophylaxis, QRS duration, CRT response, left bundle branch block, right ventricular lead position and factors with $P < 0.1$ in the univariate analyses were included in the multivariate analysis model. The bilateral $P < 0.05$ was considered statistically significant.

Results

Baseline data

A total of 384 patients were enrolled in this study. Twelve patients who lacked 1st-year echocardiography or ICD follow-up data were excluded. A total of 15 patients with right ventricular lead positions at the ventricular high septum, low septum, and right ventricular free wall were excluded. Five patients with the left ventricular lead position at the apex were excluded. A total of 352 patients were finally enrolled in this study [Figure 2].

These 352 patients were divided into the RVMS group with 155 patients (44.0%) and the RVA group with 197 patients (56.0%). The baseline data including ischemic cardiomyopathy, primary prophylaxis, and distribution of left ventricular leads of patients did not have significant differences between the two groups ($P > 0.05$) [Table 1].

Effect of right ventricular lead position on VTA and mortality

Twelve months after implantation, 62.8% of patients had LVEF improvement >10%. The response rates between RVMS group and RVA group were similar (62.6% vs. 62.9%, $\chi^2 = 0.01$, $P = 0.94$). The 2-year VTA-free survival of patients was not significantly different between the two groups, and the mortality between the two groups was similar [Figure 3]. The results of the Cox multivariate analysis suggested that ischemic cardiomyopathy (hazard ratio [*HR*] = 1.78, 95% confidence interval [*CI*]:1.25–2.54, $P < 0.01$), primary prophylaxis (*HR* = 0.57, 95% *CI*: 0.41–0.79, $P < 0.01$), and CRT response (*HR* = 0.43, 95% *CI*: 0.31–0.60, $P < 0.01$) were influencing factors of VTA, whereas the right ventricular lead position did not affect VTA (*HR* = 0.99, 95% *CI*: 0.71–1.38, $P = 0.94$).

Effects of different right ventricular lead and left ventricular lead combination on myocardial remodeling and VTA

The left ventricular leads included 62 patients of ALCV (17.6%), 205 patients of LCV (58.2%), and 85 patients

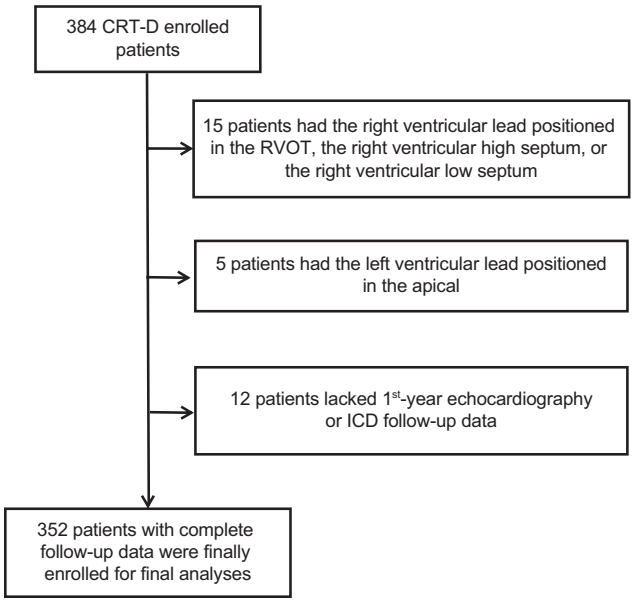

Figure 2: Flowchart of the study on influence of the right ventricular lead location in cardiac resynchronization therapy. CRT-D: Cardiac resynchronization therapy-defibrillator; RVOT: Right ventricular outflow tract; ICD: Implantable cardioverter defibrillator.

Table 1: Baseline characteristics of patients with a CRT-D in the RVA and RVMS groups

Characteristics	RVMS (n = 155)	RVA (n = 197)	Statistics	P
Age (years), mean ± SD	59.9 ± 13.1	61.6 ± 11.8	−1.29*	0.20
Female, n (%)	48 (31.0)	56 (28.4)	0.20†	0.60
Ischemic cardiomyopathy, n (%)	38 (24.5)	51 (25.9)	0.09†	0.77
Primary prophylaxis, n (%)	104 (67.1)	128 (65.0)	0.17†	0.68
NYHA class, n (%)				
II	12 (7.7)	21 (10.7)	−0.18‡	0.86
III	101 (65.2)	116 (58.9)		
IV	42 (27.1)	60 (30.5)		
LVEF (%), mean ± SD	26.0 ± 5.2	26.0 ± 5.4	−0.91*	0.93
LVEDV (ml), mean ± SD	280.1 ± 81.1	280.2 ± 79.3	−0.05*	0.96
LVESV (ml), mean ± SD	208.1 ± 64.8	208.8 ± 65.2	−0.11*	0.92
QRS duration (ms), mean ± SD	159.0 ± 25.2	154.3 ± 24.4	1.73*	0.08
LBBB, n (%)	103 (66.5)	129 (65.5)	0.04†	0.85
Diabetes, n (%)	32 (20.6)	52 (26.4)	1.58†	0.21
Renal failure, n (%)	26 (16.8)	39 (19.8)	0.53†	0.47
Hypertension, n (%)	105 (67.7)	121 (61.4)	1.51†	0.22
β-blockers, n (%)	135 (87.1)	176 (89.3)	0.42†	0.52
ACEI or ARB, n (%)	130 (83.9)	172 (87.3)	0.84†	0.36
Aldosterone, n (%)	107 (69.0)	134 (68.0)	0.04†	0.84
Amiodarone, n (%)	25 (16.1)	33 (16.8)	0.02†	0.88
LV lead position, n (%)				
ALCV	24 (15.5)	38 (19.3)	1.32†	0.52
LCV	90 (58.1)	115 (58.4)		
PLCV	41 (26.5)	44 (22.3)		

Values are presented as mean ± SD or n (%). *Student's t-test; †Chi-square test; ‡Wilcoxon Mann-Whitney test. NYHA: New York Heart Association; LVEF: Left ventricular ejection fraction; LVEDV: Left ventricle end-diastolic volume; LVESV: Left ventricle end-systolic volume; LBBB: Left bundle branch block; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; ALCV: Anterolateral cardiac vein; LCV: Lateral cardiac vein; PLCV: Posterolateral cardiac vein; SD: Standard deviation; CRT-D: Cardiac resynchronization therapy-defibrillator; RVA: Right ventricular apical; RVMS: Right ventricular middle septum; LV: Left ventricular.

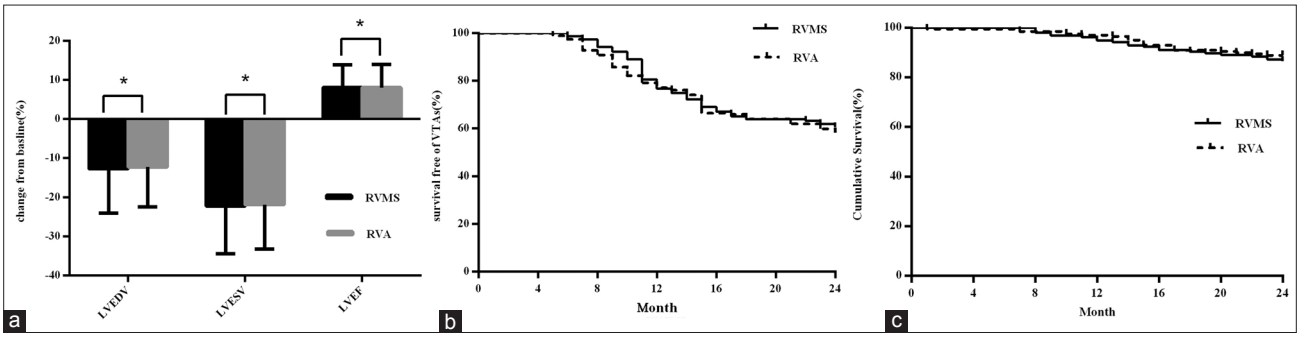

Figure 3: Effect of right ventricular lead position on VTA and mortality in RVMS location (n = 155) and RVA lead location (n = 197). Echocardiography response at 12-month follow-up of in patients with RVMS location vs. RVA lead location, *P > 0.05 (a). Survival free of VTA in the RVMS and RVA after 24-month follow-up, unadjusted P = 0.65 (b). Survival free of death in the RVMS and RVA group after 24-month follow-up, unadjusted P = 0.50 (c). LVEDV: Left ventricle end-diastolic volume; LVESV: Left ventricle end-systolic volume; LVEF: Left ventricular ejection fraction; RVMS: Right ventricular middle septum; RVA: Right ventricular apical; VTA: Ventricular arrhythmias.

of PLCV (24.2%), the response rate was not significant in these three groups (56.5% vs. 66.8% vs. 58.1%, χ^2 = 0.28, P = 0.18). In the subgroup analysis, when the left ventricular lead was positioned at the ALCV, the response rate and VTA at 12 months in the RVMS group were worse than in the RVA group (41.7% vs. 68.4%, χ^2 = 4.32, P = 0.04 and 66.7% vs. 28.9%, χ^2 = 8.51, P < 0.01, respectively). When the left ventricular lead was at the LCV, there were no differences between these two groups in regard to response rate or VTA (65.6% vs. 67.8%, χ^2 = 0.12, P = 0.73 and 32.2% vs. 36.5%, χ^2 = 0.41, P = 0.52, respectively). When the left ventricular lead was at the PLCV, the results in the RVMS group were better than those in the RVA group (68.3% vs. 45.4%, χ^2 = 4.50, P = 0.03 and 39.0% vs. 65.9%, χ^2 = 6.16, P = 0.01, respectively) [Table 2]. The further multivariate analysis results suggested that when the left ventricular lead was positioned at the ALCV, the risk of VTA (HR = 3.29, 95% CI: 1.33–8.16, P = 0.01) and appropriate defibrillation (HR = 4.33, 95% CI: 1.64–11.40, P < 0.01) in the RVMS group increased [Figure 4a-4c]. When the left ventricular lead was positioned

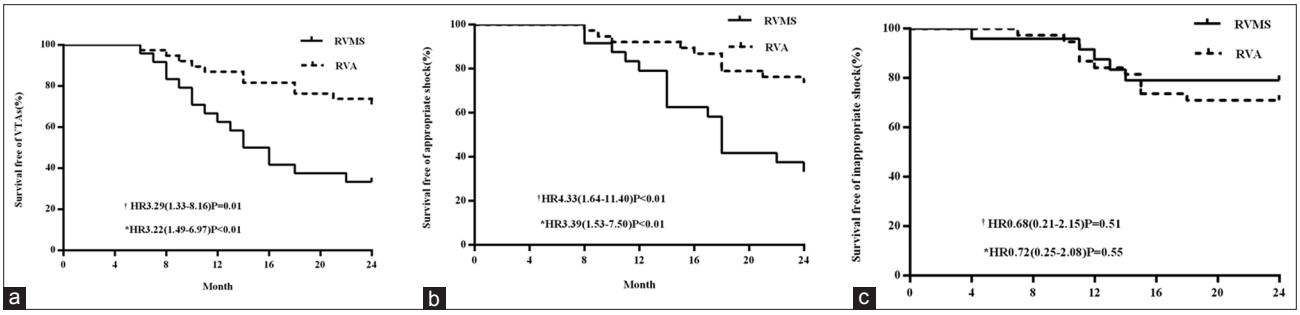

Figure 4: Kaplan-Meier analysis of survival free of VTA (a), appropriate shock (b), and inappropriate shock (c) by RVMS and RVA in the ALCV cohort. *Univariate Cox proportional hazards analysis; †Multivariate Cox proportional hazard analysis. RVMS: Right ventricular middle septum; RVA: Right ventricular apical; VTA: Ventricular arrhythmias; ALCV: Anterolateral cardiac vein; HR: Hazard ratio.

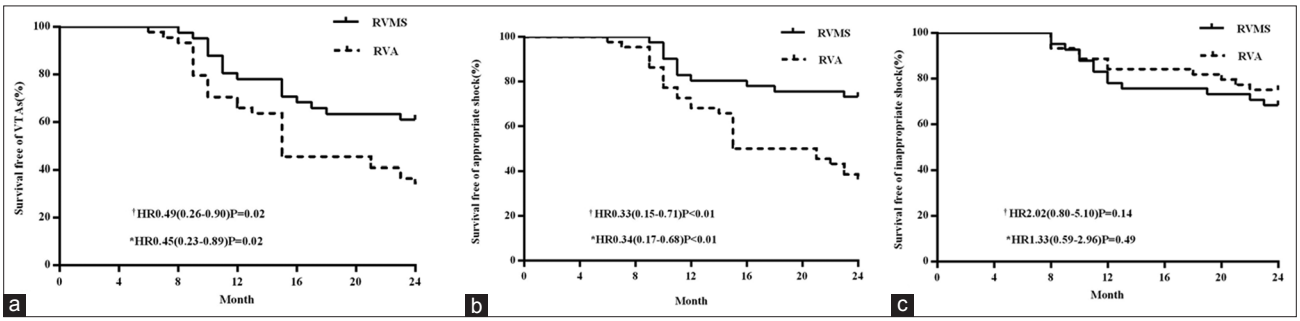

Figure 5: Kaplan-Meier analysis of survival free of VTA (a), appropriate shock (b), and inappropriate shock (c) by RVMS and RVA in the PLCV cohort. *Univariate Cox proportional hazard analysis; †Multivariate Cox proportional hazard analysis. RVMS: Right ventricular middle septum; RVA: Right ventricular apical; VTA: Ventricular arrhythmias; PLCV: Posterolateral cardiac vein; HR: Hazard ratio.

at the PLCV, the risk of VTA (*HR* = 0.45, 95% *CI*: 0.23–0.89, *P* = 0.02) and appropriate defibrillation (*HR* = 0.33, 95% *CI*: 0.15–0.71, *P* < 0.01) in the RVMS group decreased [Figure 5a-5c]. When the left ventricular lead was positioned at the LCV, the risk of VTA (*HR* = 0.93, 95% *CI*: 0.58–1.51, *P* = 0.78) and appropriate defibrillation (*HR* = 1.20, 95% *CI*: 0.69–2.09, *P* = 0.51) between the RVMS and RVA groups was similar. Inappropriate defibrillation among all combinations of leads did not have a significant difference between groups (*P* > 0.05).

Discussion

By comparing the influence of different right ventricular lead positions on VTA after CRT, we obtained the following results: (1) without considering the left ventricular lead position, only analysis of the right ventricular lead positions was performed, and the results showed that the risks of VTA and appropriate defibrillation between the RVMS and RVA groups were similar; (2) when the left ventricular lead was at the ALCV or the PLCV, the respective performances of the RVA and RVMS groups were differences, and the risk of VTA and appropriate defibrillation was reduced when a farther right ventricular lead was chosen. However, when the left ventricular lead was at the LCV, there were no differences; (3) the right ventricular lead position did not have significant effects on inappropriate defibrillation.

Three previous large-scale studies compared the influence of the right ventricular lead location on VTA of CRT patients but obtained conflicting results. A subgroup study of the MADIT-CRT trial showed that the risk of VTA increased in the 1st year in the non-RVA (NRVA) group.[10] A subsequent Danish study showed that appropriate treatment was delivered significantly more often in the RVA group than in the NRVA group.[11] The subgroup analysis of the SPICE trial,[12] which used the right ventricular lead for random grouping, showed neither a reduction in VTA and appropriate defibrillation nor an increased in the RVMS group. Our study simply divided patients into RVMS and RVA groups, and the conclusion was similar to that reported in the SPICE trial. However, opposite results were obtained in the other two studies. The variation in the results might be due to the differences in the baseline data of the samples. In addition, the nonrandom grouping based on the right ventricular leads introduced selection bias that caused an unbalanced distribution of the sample sizes between the NRVA group and the RVA group (the NRVA group in the MADIT-CRT trial only accounted for 12% of patients).

It is worth noting that although the MADIT-CRT trial showed that NRVA increased the risk of arrhythmia, the risk was reduced in the 2nd year. The reason might be due to the gradual reduction of repolarization dispersion in patients with the improvement in myocardial remodeling; therefore, the arrhythmic effect was offset by the antiarrhythmic effect. Another subgroup study in the MADIT-CRT trial grouped patients according to the degree of cardiac function improvement and showed that the incidence of the first VTA within 2 years in the CRT-D super-response group

Table 2: Echocardiography response, VTA, appropriate shock, and inappropriate shock in patients with RVMS and RVA leads corresponding to different LV lead position

Items	ALCV		χ^2	*P*	LCV		χ^2	*P*
	RVMS (*n* = 24)	RVA (*n* = 38)			RVMS (*n* = 90)	RVA (*n* = 115)		
Response (%)	41.7	68.4	4.32	0.04	65.6	67.8	0.12	0.73
VTA (%)	66.7	28.9	8.51	<0.01	32.2	36.5	0.41	0.52
Appropriate shock (%)	66.7	26.3	9.84	<0.01	26.7	25.2	0.06	0.81
Inappropriate shock (%)	20.8	28.9	0.51	0.48	24.4	23.5	0.03	0.87
Items	**PLCV**		χ^2	*P*	**Total**		χ^2	*P*
	RVMS (*n* = 41)	RVA (*n* = 44)			RVMS (*n* = 155)	RVA (*n* = 197)		
Response (%)	68.3	45.4	4.50	0.03	62.6	62.9	0.01	0.94
VTA (%)	39.0	65.9	6.16	0.01	39.3	41.6	0.19	0.67
Appropriate shock (%)	26.8	63.6	11.58	<0.01	32.9	34.0	0.05	0.83
Inappropriate shock (%)	31.7	25.0	0.47	0.49	25.8	24.9	0.04	0.84

ALCV: Anterolateral cardiac vein; LCV: Lateral cardiac vein; PLCV: Posterolateral cardiac vein; RVMS: Right ventricular middle septum; RVA: Right ventricular apical; VTA: Ventricular arrhythmias; LV: Left ventricular.

was significantly lower than that in the simple ICD group and the CRT-D low-response group. In addition, with the reversal of myocardial remodeling, with every 10% reduction in LVESV, the risk of VF was reduced by 21%, and the number of appropriate defibrillations significantly decreased.[5] Schaer *et al*.[19] and Van Boven *et al*.[20] showed that patients with cardiac function improvement of LVEF >35% had a significantly reduced number of ICDs. Patients who responded to CRT had a clearer reduction in the risk of VTA.[6] Whether the right ventricular lead position affects myocardial remodeling in CRT patients may partially determine the risk of the development of VTA. So is there a better right ventricular lead position than the RVA? A small-sample, nonrandomized study by Riedlbauchová *et al*.[21] with 99 subjects showed that RVMS pacing could significantly reduce LVEDV. Unfortunately, the majority of relevant studies did not show that the NRVA pacing location could improve myocardial remodeling;[10,12,21] of these studies, the subgroup analysis in the SEPTAL CRT study only showed that the NRVA was not worse than the RVA.[22] The SPICE trial also did not show that the RVMS had an advantage on myocardial remodeling,[12] which might be the reason why the SPICE trial did not show an effect of the right ventricular lead on arrhythmias.

In contrast to conventional pacemakers, CRT depends on the collaborative work of the left and right ventricular leads to increase cardiac synchronization. The simple consideration of the right ventricular lead position has some limitations, and therefore, we further analyzed the influence of the right ventricular lead position on myocardial remodeling and VTA under different left ventricular lead positions. The results showed that compared with the RVA group at the ALCV, the RVMS had lower response rates; compared with the RVMS group at the PLCV, the RVA group had lower response rates, and the performances of these two groups at the LCV were similar. These results were consistent with previous study results. Some studies compared different combinations of the left and right ventricular leads and showed that the distance between the left and right ventricular leads or the electrical separation might influence the response to CRT.[13,23] The response of the lead combinations improved for greater lead distances. When the left ventricular lead was positioned at the ALCV or the PLCV, the right ventricular lead position had different influences on myocardial remodeling. The improvement in myocardial remodeling might influence the development of VTA. We further compared the influence of the right ventricular leads between the two groups on arrhythmias and appropriate defibrillation under different left ventricular lead conditions. The results showed that the RVA was better than the RVMS when left ventricular lead was positioned at the ALCV, and the RVMS was better than the RVA when left ventricular lead was at the PLCV; however, there was no effect on inappropriate defibrillation. Some studies suggest that high VTA rate is associated with the apex or anterior left ventricular lead position,[9] while our study shows that there is no significant difference between the anterior or lateral and posterior groups in the influence on VTA after CRT; however, in the ALCV subgroup, the risk of VTA was lower when right ventricular lead was positioned in RVA, while the response rate was higher. We speculate that the different VTA rate between RVA and RVMS may be due to the different response rate. Therefore, the distance between the left and right ventricular leads might influence not only myocardial remodeling but also electrical remodeling.

Because of myocardial scars and vascular anatomical factors, CRT-D patients might not be able to freely receive left ventricular lead implantation. This study showed that when the left ventricular lead was implanted into the ALCV or the PLCV, the selection of the right ventricular lead position had a greater influence on both myocardial remodeling and arrhythmias in patients; therefore, implantation of the right ventricular lead into inappropriate locations should be avoided. However, when the left ventricular lead is positioned at the LCV, the right ventricular lead can be implanted into either the RVA or the RVMS, and more options are available, which may be one of the reasons

why the majority of current studies all showed that the best location of the left ventricular lead is the LCV.[12]

This study was a retrospective study. The lead was not implanted randomly; therefore, implantation of the left and right ventricular leads might be associated with selection bias, and a lower percentage of leads was positioned at the ALCV. The conventional localization method was used for the RVMS and was confirmed by a third party; however, due to technical limitations, this method might not be accurate. In this study, the prevalence of ischemic cardiomyopathy was low, whether the same conclusion can be obtained for ischemic cardiomyopathy and nonischemic cardiomyopathy is unclear. Similarly, determining whether there are differences in primary prophylaxis, secondary prophylaxis, or gender still requires large-scale, randomized controlled studies in the future.

In conclusion, when the left ventricular lead was positioned at the ALCV or the PLCV, the right ventricular lead position was associated with the development of VTA after CRT and appropriate defibrillation. Positioning the right ventricular lead at the RVA and the RVMS respectively can help to reduce this risk.

Financial support and sponsorship

This study was supported by a grant from the Central Guidance for Local Science and Technology Development Program Special Funds (No. 2016080802D113).

Conflicts of interest

There are no conflicts of interest.

References

1. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, *et al.* The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med 2005;352:1539-49. doi: 10.1056/NEJMoa050496.
2. Roger VL, Weston SA, Redfield MM, Hellermann-Homan JP, Killian J, Yawn BP, *et al.* Trends in heart failure incidence and survival in a community-based population. JAMA 2004;292:344-50. doi: 10.1001/jama.292.3.344.
3. Smer A, Saurav A, Azzouz MS, Salih M, Ayan M, Abuzaid A, *et al.* Meta-analysis of risk of ventricular arrhythmias after improvement in left ventricular ejection fraction during follow-up in patients with primary prevention implantable cardioverter defibrillators. Am J Cardiol 2017;120:279-86. doi: 10.1016/j.amjcard.2017.04.020.
4. Ruwald MH, Solomon SD, Foster E, Kutyifa V, Ruwald AC, Sherazi S, *et al.* Left ventricular ejection fraction normalization in cardiac resynchronization therapy and risk of ventricular arrhythmias and clinical outcomes: Results from the multicenter automatic defibrillator implantation trial with cardiac resynchronization therapy (MADIT-CRT) trial. Circulation 2014;130:2278-86. doi: 10.1161/CIRCULATIONAHA.114.011283.
5. Barsheshet A, Wang PJ, Moss AJ, Solomon SD, Al-Ahmad A, McNitt S, *et al.* Reverse remodeling and the risk of ventricular tachyarrhythmias in the MADIT-CRT (Multicenter automatic defibrillator implantation trial-cardiac resynchronization therapy). J Am Coll Cardiol 2011;57:2416-23. doi: 10.1016/j.jacc.2010.12.041.
6. Itoh M, Yoshida A, Fukuzawa K, Kiuchi K, Imamura K, Fujiwara R, *et al.* Time-dependent effect of cardiac resynchronization therapy on ventricular repolarization and ventricular arrhythmias. Europace 2013;15:1798-804. doi: 10.1093/europace/eut145.
7. Lellouche N, De Diego C, Boyle NG, Wiener I, Akopyan G, Child JS, *et al.* Relationship between mechanical and electrical remodelling in patients with cardiac resynchronization implanted defibrillators. Europace 2011;13:1180-7. doi: 10.1093/europace/eur106.
8. Thébault C, Donal E, Meunier C, Gervais R, Gerritse B, Gold MR, *et al.* Sites of left and right ventricular lead implantation and response to cardiac resynchronization therapy observations from the REVERSE trial. Eur Heart J 2012;33:2662-71. doi: 10.1093/eurheartj/ehr505.
9. Kutyifa V, Zareba W, McNitt S, Singh J, Hall WJ, Polonsky S, *et al.* Left ventricular lead location and the risk of ventricular arrhythmias in the MADIT-CRT trial. Eur Heart J 2013;34:184-90. doi: 10.1093/eurheartj/ehs334.
10. Kutyifa V, Bloch Thomsen PE, Huang DT, Rosero S, Tompkins C, Jons C, *et al.* Impact of the right ventricular lead position on clinical outcome and on the incidence of ventricular tachyarrhythmias in patients with CRT-D. Heart Rhythm 2013;10:1770-7. doi: 10.1016/j.hrthm.2013.08.020.
11. Kronborg MB, Johansen JB, Haarbo J, Riahi S, Philbert BT, Jørgensen OD, *et al*. Association between implantable cardioverter-defibrillator therapy and different lead positions in patients with cardiac resynchronization therapy. EP Europace 2018;20:133-9. doi: 10.1093/europace/eux296.
12. Asbach S, Lennerz C, Semmler V, Grebmer C, Solzbach U, Kloppe A, *et al*. Impact of the right ventricular lead position on clinical end points in CRT recipients – A subanalysis of the multicenter randomized SPICE trial. Pacing Clin Electrophysiol 2016;39:261-7. doi: 10.1111/pace.12793.
13. Miranda RI, Nault M, Johri A, Simpson CS, Michael KA, Abdollah H, *et al.* Maximal electric separation-guided placement of right ventricular lead improves responders in cardiac resynchronization defibrillator therapy. Circ Arrhythm Electrophysiol 2012;5:927-32. doi: 10.1161/CIRCEP.111.967208.
14. Haghjoo M, Bonakdar HR, Jorat MV, Fazelifar AF, Alizadeh A, Ojaghi-Haghjghi Z, *et al.* Effect of right ventricular lead location on response to cardiac resynchronization therapy in patients with end-stage heart failure. Europace 2009;11:356-63. doi: 10.1093/europace/eun375.
15. Kolb C, Tzeis S, Andrikopoulos G, Asbach S, Lemke B, Hansen C, *et al.* Rationale and design of the SPICE study-septal positioning of ventricular ICD electrodes. J Interv Card Electrophysiol 2011;31:247-54. doi: 10.1007/s10840-011-9575-z.
16. Wilkoff BL, Ousdigian KT, Sterns LD, Wang ZJ, Wilson RD, Morgan JM, *et al.* A comparison of empiric to physician-tailored programming of implantable cardioverter-defibrillators: Results from the prospective randomized multicenter EMPIRIC trial. J Am Coll Cardiol 2006;48:330-9. doi: 10.1016/j.jacc.2006.03.037.
17. Wilkoff BL, Williamson BD, Stern RS, Moore SL, Lu F, Lee SW, *et al.* Strategic programming of detection and therapy parameters in implantable cardioverter-defibrillators reduces shocks in primary prevention patients: Results from the PREPARE (Primary prevention parameters evaluation) study. J Am Coll Cardiol 2008;52:541-50. doi: 10.1016/j.jacc.2008.05.011.
18. Sapp JL, Parkash R, Wells GA, Yetisir E, Gardner MJ, Healey JS, *et al.* Cardiac resynchronization therapy reduces ventricular arrhythmias in primary but not secondary prophylactic implantable cardioverter defibrillator patients: Insight from the resynchronization in ambulatory heart failure trial. Circ Arrhythm Electrophysiol 2017;10: e004875. doi: 10.1161/CIRCEP.116.004875.
19. Schaer BA, Osswald S, Di Valentino M, Soliman OI, Sticherling C, ten Cate FJ, *et al.* Close connection between improvement in left ventricular function by cardiac resynchronization therapy and the incidence of arrhythmias in cardiac resynchronization therapy-defibrillator patients. Eur J Heart Fail 2010;12:1325-32. doi: 10.1093/eurjhf/hfq171.
20. Van Boven N, Bogaard K, Ruiter J, Kimman G, Theuns D, Kardys I, *et al.* Functional response to cardiac resynchronization therapy is associated with improved clinical outcome and absence of appropriate shocks. J Cardiovasc Electrophysiol 2013;24:316-22. doi: 10.1111/jce.12037.

21. Riedlbauchová L, Cihák R, Bytesník J, Vancura V, Frídl P, Hosková L, *et al.* Optimization of right ventricular lead position in cardiac resynchronisation therapy. Eur J Heart Fail 2006;8:609-14. doi: 10.1016/j.ejheart.2005.11.009.
22. Leclercq C, Sadoul N, Mont L, Defaye P, Osca J, Mouton E, *et al.* Comparison of right ventricular septal pacing and right ventricular apical pacing in patients receiving cardiac resynchronization therapy defibrillators: The SEPTAL CRT study. Eur Heart J 2016;37:473-83. doi: 10.1093/eurheartj/ehv422.
23. Shimano M, Inden Y, Yoshida Y, Tsuji Y, Tsuboi N, Okada T, *et al.* Does RV lead positioning provide additional benefit to cardiac resynchronization therapy in patients with advanced heart failure? Pacing Clin Electrophysiol 2006;29:1069-74. doi: 10.1111/j.1540-8159.2006.00500.x.

心脏再同步治疗右室导线位置选择对室性心律失常的影响

摘要

背景：右室导线位置对心脏再同步治疗（cardiac resynchronization therapy，CRT）后室性心律失常（ventricular arrhythmias，VTA）的影响并不明确，为此本研究评价CRT右室导线位于右室中位间隔部（right ventricular middle septum, RVMS）和右室心尖部（right ventricular apical, RVA）对于VTA的影响。

方法：选取我院心脏中心2012年5月至2016年7月行心脏再同步治疗和植入式除颤器（cardiac resynchronization therapy defibrillator，CRT-D）治疗的患者352例，统计2年的临床随访资料和起搏器随访资料，根据右室导线位置的不同分为RVMS组和RVA组，通过Kaplan-Meier曲线和COX多因素分析评价右室导线位置对VTA的影响。

结果：不考虑左室导线位置时，RVMS组和RVA组对VTA无影响。但亚组分析发现当左室导线位于前侧静脉（anterolateral cardiac vein，ALCV）时，RVMS有增加VTA、恰当除颤风险（*HR*=3.29, *P*=0.01 和 *HR*=4.33, *P*<0.01），当左室导线为后侧静脉（posterolateral cardiac vein，PLCV）时，RVMS组风险降低（*HR*=0.45, *P*=0.02和*HR*=0.33, *P*<0.01），当左室导线为外侧静脉（lateral cardiac vein，LCV）时，两组间无明显差异。对于不恰当除颤，各组之间均无明显差异。

结论：左室导线为ALCV和PLCV时，右室导线位置与CRT后VTA的发生和恰当除颤相关。较远的导线间距离除了进一步改善心功能外还有可能降低VTA的风险。