# Is Right Ventricular Outflow Tract Pacing Superior to Right Ventricular Apex Pacing in Patients with Normal Cardiac Function?

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ABSTRACT

*Background:* Whether right ventricular outflow tract (RVOT) pacing is superior to right ventricular apex (RVA) pacing in terms of ventricular synchrony, cardiac function, and remodeling in patients with normal cardiac function is still unknown.

*Hypothesis:* Right ventricular outflow tract pacing is superior to RVA pacing in patients with normal cardiac function.

*Methods:* A total of 96 consecutive patients with high or third-degree atrial ventricular block were enrolled and randomized into 2 groups: RVOT pacing group (n = 48) and RVA pacing group (n = 48). Tissue Doppler imaging (TDI) and 2D echocardiography were performed to study left ventricular (LV) systolic and diastolic synchrony, LV volumes, and function.

*Results:* There were no significant differences in baseline characteristics between the 2 groups. Left ventricular systolic asynchrony is more severe in the RVA pacing group than in the RVOT pacing group ($P < 0.05$), while diastolic synchrony is not significantly (NS) different between the 2 groups after pacing. There were no significant differences with respect to the mean myocardial systolic (Sm) and early diastolic velocities (Em), LV ejection fraction, LV end-diastolic and systolic volume in the 2 groups at 12 months of follow-up (all NS).

*Conclusions:* Although RVOT pacing caused more synchronous LV contraction compared with RVA pacing, it had no benefit over RVA pacing in aspect of preventing cardiac remodeling and preserving LV systolic function after 12 months of pacing in patients with normal cardiac function.

## Introduction

In patients treated with permanent cardiac pacing, the ventricular electrode is typically placed in the right ventricular apex (RVA) since it provides excellent lead stability and low capture thresholds. In recent years, we have recognized that RVA pacing changes ventricular activation sequences, causes ventricular dyssynchrony, impairs cardiac function, and thus increases the risk of new onset heart failure and mortality.[1–3] With the development of active electrodes, there have been more and more studies aimed at looking for better alternative pacing sites. A quantitative review by de Cock et al[4] in 2003, analyzed 9 published randomized studies and other acute and midterm studies,[5–7] and found that right ventricular outflow tract (RVOT) pacing had been shown to have more beneficial left ventricular (LV) hemodynamics than RVA pacing. But the results were controversial and most of the studies used conventional echocardiography to evaluate the effect on cardiac function and hemodynamics. Up to now, most of the studies comparing RVOT and RVA pacing have enrolled patients with poor cardiac function or varied cardiac functions. There were still limited studies[8–10] comparing the effect of RVOT and RVA pacing on cardiac function and remodeling in patients with normal cardiac function. Just a few studies[8,11] compared the effect of RVOT and RVA pacing on ventricular synchrony and no study compared diastolic synchrony between RVOT and RVA pacing. Tissue Doppler imaging (TDI), a relatively new technology, can be used to evaluate global cardiac function[12] and ventricular synchrony.[13,14] Using standard 2D echocardiography (2DE) and TDI, this prospective randomized control study aimed to systematically evaluate the effects of RVOT and RVA pacing on left ventricular synchrony, cardiac function, and remodeling in patients with normal cardiac function.

## Methods

### Patient Selection

A total of 96 consecutive patients with high or complete atrial ventricular block necessitating permanent pacemaker implantation were prospectively enrolled. The inclusion criteria were as follows: (1) the patients should be over 18 years of age; (2) left ventricular ejection fraction (LVEF) > 50%; and (3) the patients should not have clinical manifestations of congestive heart failure. Patients were randomized into 2 groups: group A (RVOT pacing patients,

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n = 48) and group B (RVA pacing patients, n = 48). The study conformed to the principles outlined in the Declaration of Helsinki. The local ethics committee approved the study and all patients provided written informed consent to participate in the study.

### Pacemaker Implantation

All patients were implanted with dual-chamber pacemakers. All leads were transvenously inserted from the left or right subclavian vein. The atrial leads were placed at the right atrial appendage. In group B, the passive fixated electrodes were positioned toward the right ventricular apex. In group A, the helix electrodes were positioned against the mid-septum of the RVOT, as verified by multiple fluoroscopic views and ECG, and then screwed into the myocardiom with the ECG demonstrating an upward axis in the II, III, aVF, and an inferior axis in I. All the ventricular leads were positioned with the narrowest QRS complex available, the lowest pacing threshold, and the highest local amplitude. The atrioventricular delay (AVD) was programmed to the optimal value as determined by the method our previous study reported.[15]

### Echocardiography and TDI

Patients were imaged with a commercially available system (Vingmed Vivid Seven, GE Vingmed, Milwaukee, WI) equipped with 3.5-MHz transducer. All echocardiographic examinations were performed and analyzed by the same experienced echocardiographer, who was blinded to clinical data and group division. Echocardiographic measurements were done within 24 hours before pacemaker implantation and after 12 months. In all patients, the acoustic window was adequate, yielding good image quality; 2DE and color TDI were acquired. At least 3 consecutive beats were stored for off-line analysis. Using the 2DE, we acquired the LV end-diastolic (LVEDV) and end-systolic volume (LVESV) and LVEF measured by the modified biplane Simpson's rule. Color TDIs were acquired in apical 4-chamber, 3-chamber, and 2-chamber views. To avoid aliasing, the color-coded area and the settings of the echocardiographic equipment were adjusted to obtain the highest possible frame rate ($\geq$130 frames/s). Analysis was carried out in the model of 12 segments.[13] From the color TDI, the time to peak myocardial systolic velocity during the ejection phase (Ts) and the time to peak myocardial early diastolic velocity (Te) were measured with reference to QRS complex, the peak myocardial systolic, and peak myocardial early diastolic velocities were recorded. For the assessment of systolic synchrony, the standard deviation of Ts (Ts-SD) of all 12 LV segments and the maximal difference in Ts (Ts-diff) between any 2 of the 12 LV segments were calculated.[13,14] For evaluation of diastolic synchrony, the standard deviation of Te (Te-SD) of all 12 LV segments and the maximal difference in Te (Te-diff) were measured.[13,14] To assess global cardiac function, the mean myocardial systolic (Sm) and early diastolic (Em) velocities of 12 segments were calculated. The intraobserver's correlations for these variables were compared in 20 consecutive measurements and showed satisfactory reproducibility (intraobserver variability of Ts-SD, Te-SD, Ts-dif, Sm, and Em was 6.85%, 6.46%, 5.65%, 4.89%, and 4.68%, respectively).

### Statistical Analyses

Continuous data were expressed as mean $\pm$ SD, otherwise as median (first and third quartile). A paired Student *t* test analysis was used for comparison within groups and a non-paired Student *t* test analysis for comparison between groups, all were done as 2-sided tests. Covariance analyses were used to compare variables between the 2 groups (LVEF, LVEDV, LVESV, Sm, and Em) with adjustment for the pre-pacing values of these variables. A $P$ value $<0.05$ was considered statistically significant. All statistical analyses were completed by using SPSS 11.5 software package (SPSS, Inc, Chicago, IL).

## Results

### Baseline Characteristics

Two patients in group A and 4 patients in group B were lost during the 12 months of follow-up. The rest were included in the analysis. There were no significant differences between the 2 groups in age, gender, underlying disease, bradyarrhythmia, New York Heart Association (NYHA) functional class, cumulative percentage of ventricular pacing or atrial pacing, and optimal atrioventricular delay (Table 1). The baseline QRS duration did not differ significantly between group A and B ($96.75 \pm 9.56$ vs $97.23 \pm 8.89$ ms, not significant [NS]). But after pacemaker implantation, the paced QRS duration was shorter in group A than in group B ($161.07 \pm 22.36$ vs $177.14 \pm 22.52$ ms, $P < 0.05$).

### Pacemaker Implantation and Complications

All pacemakers were successfully implanted in both groups. x-ray time was longer in group A than in group B ($186.2 \pm 370.3$ s vs $96.0 \pm 149.6$ s, $P < 0.05$). There were no complications such as lead dislocation, purse infection, bad pacing, or sensing in the 2 groups.

### Left Ventricular Synchronization

Ts-SD, Te-SD, Ts-diff, and Te-diff were not different between group A and group B at baseline (all NS, Table 2). After 12 months of ventricular pacing, Ts-SD ($26.43 \pm 14.39$ vs $35.53 \pm 15.53$ ms, $P < 0.05$) and Te-SD ($23.82 \pm 8.90$ vs $27.98 \pm 11.07$ ms, $P < 0.05$; Table 2) increased in group B and remained unchanged in group A (Ts-SD: $24.98 \pm 15.49$ vs $28.30 \pm 15.09$ ms; Te-SD: $25.84 \pm 14.69$ vs $28.31 \pm 10.12$ ms; both NS; Table 2). Ts-diff was prolonged (group A: $71.25 \pm 30.61$ vs $89.53 \pm 35.72$ ms; group B: $74.58 \pm 29.52$ vs $108.64 \pm 36.06$ ms; both $P < 0.05$; Table 2) and Te-diff did not change (group A: $75.83 \pm 42.12$ vs


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Table 1. Clinical Characteristics of Both Groups

| | RVOT Group | RVA Group | *P* Value |
|---|---|---|---|
| Patients completing follow-up | 46 | 44 | |
| Age (yrs) | 69 ± 13 | 70 ± 11 | NS |
| Gender (male/female) | 27/19 | 25/19 | NS |
| Cumulative percentage of ventricular pacing (%) | 98.2% | 97.3% | NS |
| Cumulative percentage of atrial pacing (%) | 5.52% | 4.59% | NS |
| Optimal atrioventricular delay (ms) | 109.26 ± 28.72 | 121.35 ± 34.00 | NS |
| Underlying disease | | | |
| Ischemic heart disease | 7 | 8 | NS |
| Hypertension | 29 | 27 | NS |
| Diabetes | 6 | 5 | NS |
| NYHA functional class | | | |
| I/II/III/IV | 36/10/0/0 | 35/9/0/0 | NS |
| Baseline QRS duration (ms) | 96.75 ± 9.56 | 97.23 ± 8.89 | NS |
| Paced QRS duration (ms) | 161.07 ± 22.36 | 177.14 ± 22.52 | <.05 |

Abbreviations: NS, not significant; NYHA, New York Heart Association; RVA, right ventricular apex; RVOT, right ventricular outflow tract.

78.14 ± 31.03 ms; group B: 73.96 ± 29.59 vs 75.68 ± 30.83 ms; both NS; Table 2) in both groups. Ts-SD and Ts-diff in group B were greater than those in group A (both $P < 0.05$, Table 2), while Te-SD and Te-diff were not different between the 2 groups at 12 months of follow-up (NS, Table 2).

### Left Ventricular Function

Left ventricular ejection fraction, Sm, and Em were not different between the 2 groups at baseline and 12 months of follow-up (all NS, Table 3). After 12 months of ventricular pacing, Sm (group A: 5.03 ± 1.14 vs 4.44 ± 1.08 cm/s; group B: 5.10 ± 1.56 vs 4.24 ± 1.15 cm/s; both $P < 0.05$; Table 3) and Em (group A: 5.79 ± 2.62 vs 4.43 ± 1.65 cm/s; group B: 5.42 ± 1.95 vs 4.44 ± 1.74 cm/s; both $P < 0.05$; Table 3) decreased, but LVEF did not change (group A: 68.31% ± 6.42% vs 67.64% ± 5.21%; group B: 67.92% ± 6.38% vs 65.71% ± 6.56%; both NS; Table 3) in both groups.

### Cardiac Remodeling

There was no significant difference in LVEDV and LVESV between the 2 groups before pacemaker implantation (both NS; Table 3). After 12 months of pacing, they did not change in either group A or group B (LVEDV: 81.82 ± 25.37 vs 78.14 ± 14.14 mL; 83.96 ± 19.10 vs 80.48 ± 15.04 mL; LVESV: 26.76 ± 11.25 vs 25.70 ± 6.59 mL; 27.23 ± 9.54 vs 26.70 ± 9.54 mL; all NS; Table 3) and they also did not differ between the 2 groups.

## Discussion

Our study demonstrated that RVOT pacing did not benefit over RVA pacing in the aspect of preventing cardiac remodeling and protecting LV systolic function after 12 months of pacing in patients with normal cardiac function although it caused more synchronous LV contraction compared with RVA pacing.

As seen in many previous studies,[16–18] our study showed that RVOT pacing induced shorter paced QRS duration than RVA pacing did. This result indicated that RVOT pacing resulted in better electric synchrony compared with RVA pacing. There are 2 studies comparing the mechanic synchrony between RVOT pacing and RVA pacing.[8,11] However, in the first study,[8] the indices used to evaluate ventricular mechanic asynchrony were not comprehensive or widely accepted. In the second study,[11] the sample size was very small (n = 9). Our study found that Ts-SD increased in group B and did not change in group A and that both Ts-SD and Ts-diff in group B were greater than those in group A after ventricular pacing. These results suggested that RVOT pacing induced more synchronous LV contraction than RVA pacing did. Because RVOT is close to the His-Purkinje system, RVOT pacing may mimic the physiologic electrical propagation and causes better electric-mechanic synchrony compared with RVA pacing. However, the LV diastolic synchrony between the 2 groups was not different. The possible cause is that systolic and diastolic dyssynchrony may develop through separate mechanisms.[19,20]

Our study found that after 12 months of pacing, LVEDV, LVESV, and LVEF did not change in either the RVOT pacing group or the RVA pacing group. LVEDV, LVESV, LVEF, Sm, and Em were not different between the 2 groups after 12 months of follow-up. These results indicated that RVOT pacing had no benefit over RVA pacing in the aspect of preventing cardiac remodeling and protecting LV systolic function after 12 months of pacing. It has been confirmed that it is important to protect or restore ventricular synchrony for patients with reduced LV systolic function.[21–24] However, in patients with normal LV systolic function, ventricular synchrony may be of less importance. Victor et al[7] found that in contrast to RV apical pacing,


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Table 2. Comparisons of Ventricular Synchrony Between RVA Pacing (Group B) and RVOT Pacing (Group A)

| | Group A | | Group B | | P (Pre vs Post) | | P (Group A vs B) | |
|---|---|---|---|---|---|---|---|---|
| | Pre | Post | Pre | Post | Group A | Group B | Pre | Post |
| Ts-SD (ms) | 24.98 ± 15.49 | 28.30 ± 15.09 | 26.43 ± 14.39 | 35.53 ± 15.53 | NS | <0.05 | NS | <0.05 |
| Ts-diff (ms) | 71.25 ± 30.61 | 89.53 ± 35.72 | 74.58 ± 29.52 | 108.64 ± 36.06 | <.05 | <0.05 | NS | <0.05 |
| Te-SD (ms) | 25.84 ± 14.69 | 28.31 ± 10.12 | 23.82 ± 8.90 | 27.98 ± 11.07 | NS | <0.05 | NS | NS |
| Te-diff (ms) | 75.83 ± 42.12 | 82.56 ± 35.46 | 73.96 ± 29.59 | 72.27 ± 32.34 | NS | NS | NS | NS |

Abbreviations: NS, not significant; Pre, before pacemaker implantation; Post, 12 months after pacemaker implantation; RVA, right ventricular apex; RVOT, right ventricular outflow tract; Ts-SD, standard deviation of the time to peak myocardial systolic velocity of all 12 left ventricular segments; Ts-diff, maximal difference in time to peak myocardial systolic velocity among all 12 left ventricular segments; Te-SD, standard deviation of the time to peak myocardial early diastolic velocity of all 12 left ventricular segments; Te-diff, maximal difference in time to peak myocardial early diastolic velocity among all 12 left ventricular segments.

Table 3. Comparisons of Cardiac Remodeling and Left Ventricular Systolic Function Between RVA Pacing (Group B) and RVOT Pacing (Group A)

| | Group A | | Group B | | P (Pre vs post) | | P (Group A vs B) | |
|---|---|---|---|---|---|---|---|---|
| | Pre | Post | Pre | Post | Group A | Group B | Pre | Post |
| LVEF (%) | 68.31 ± 6.42 | 67.64 ± 5.21 | 67.92 ± 6.38 | 65.71 ± 6.56 | NS | NS | NS | NS |
| Sm (cm/s) | 5.03 ± 1.14 | 4.44 ± 1.08 | 5.10 ± 1.56 | 4.24 ± 1.15 | <0.05 | <0.05 | NS | NS |
| Em (cm/s) | 5.79 ± 2.62 | 4.43 ± 1.65 | 5.42 ± 1.95 | 4.44 ± 1.74 | <0.05 | <0.05 | NS | NS |
| LVEDV (mL) | 83.12 ± 25.37 | 79.21 ± 16.31 | 84.32 ± 22.05 | 78.45 ± 17.91 | NS | NS | NS | NS |
| LVESV (mL) | 26.76 ± 11.25 | 25.70 ± 6.59 | 27.23 ± 9.54 | 26.70 ± 9.54 | NS | NS | NS | NS |

Abbreviations: Em, mean myocardial early diastolic velocity of 12 left ventricular segments; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; NS, not significant; Pre, before pacemaker implantation; Post, 12 months after pacemaker implantation; RVA, right ventricular apex; RVOT, right ventricular outflow tract; Sm, mean myocardial systolic velocity of 12 left ventricular segments.

RV septal pacing preserved LVEF in patients with baseline LVEF ≤45%, but did not gain any advantage of LVEF in patients with baseline LVEF >45%. Sweeney and Hellkamp[25] showed that in patients with normal LV systolic function without myocardial infarction, the risk of heart failure after RVA pacing was low. So RVA pacing may do little harm to patients with normal LV systolic function[26] and RVOT pacing may have no benefit over RVA pacing for these patients.

Our studies found that there was a significantly decrease of Sm and Em in both groups. But LVEF of both groups did not decrease significantly. The possible cause is that Sm and Em were more sensitive parameters to reflect ventricular function changes.[12] There were 2 reasons why Sm and Em decreased after pacing in both groups. First, before pacemaker implantation, the heart rate was low in patients with bradyarrhythmia. For meeting the body's needs, the ventricular motion was compensatorily strengthened to maintain high cardiac output. After pacemaker implantation, the ventricular motion was reinstated to normal status. Second, the ventricular motion may be impaired by ventricular pacing.[9]

## Study Limitations

We only measured dyssynchrony by Ts-SD, Ts-diff, Te-SD, Te-diff, and diastolic function by Em. Many other parameters can be used to evaluate the cardiac synchrony and function, and the parameters at present quantifying intraventricular dyssynchrony could not contain all information of dyssynchrony. Therefore, we cannot rule out the possible bias in our results. Of course, the amount of patients and the follow-up time was still not enough, results.

## Conclusion

Although RVOT pacing caused more synchronous LV contraction compared with RVA pacing, it had no benefit over RVA pacing in the aspect of preventing cardiac remodeling and protecting LV systolic function after 12 months of pacing in patients with normal cardiac function. Long-term follow up of a prospective randomized trial are awaited to see the protective value of RVOT and its clinical significance.


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