

# Right Ventricular Apical Pacing Impairs Left Ventricular Twist as Well as Synchrony: Acute Effects of Right Ventricular Apical Pacing

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**Background:** This study was designed to compare the rotation of the left ventricular (LV) apex and base, LV synchrony between LV apical and basal rotation, and LV twist, changing from intrinsic atrioventricular conduction to right ventricular apical (RVA) pacing.

**Methods:** Thirty consecutive patients with sick sinus syndrome who had undergone DDD pacemaker implantation were studied. Changing from intrinsic atrioventricular conduction to RVA pacing, the acute effect on echocardiographic parameters, including LV rotation and twist and LV apical-basal rotation delay, was assessed.

**Results:** During RVA pacing, values of peak rotation in the LV apex and base and LV twist were significantly lower than during intrinsic atrioventricular conduction ( $P = .007$ ,  $P = .003$ , and  $P < .0001$ , respectively). Apical-basal rotation delay during RVA pacing was significantly longer than during intrinsic atrioventricular conduction ( $P = .02$ ).

**Conclusions:** RVA pacing decreases apical and basal LV rotation and induces LV apical-basal rotation delay, resulting in impairment of LV twist. (J Am Soc Echocardiogr 2009;22:914-9.)

**Keywords:** Right ventricular apical pacing, Left ventricular twist, Left ventricular dyssynchrony

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## Target Audience:

This activity is designed for all cardiovascular physicians and cardiac sonographers with a primary interest and knowledge base in the field of echocardiography: in addition, residents, researchers, clinicians, intensivists, and other medical professionals with a specific interest in cardiac ultrasound will find this activity beneficial.

## Objectives:

Upon completing the reading of this article, the participants will better be able to:

1. Identify the previously-described effects of right ventricular apical pacing on left ventricular function.
2. Describe the phenomenon of left ventricular rotation at the base and apex.
3. Define the term left ventricular twist, and the role it plays in ventricular function.
4. Compare the effect of right ventricular pacing on left ventricular twist versus intrinsic atrioventricular conduction.
5. Explain the possible relationship between changes in left ventricular twist and the clinical effects of right ventricular pacing.

## Author Disclosure:

Drs. Egami, Kato, Matsuoka, Nishino, Shutta, Tanaka, Tanouchi, Yamada, and Yamaguchi all reported that they have no actual or potential conflicts of interest in relation to this program.

**Estimated Time to Complete This Activity:** 1 hour

It is well known that right ventricular apical (RVA) pacing results in asynchronous patterns of left ventricular (LV) contraction, reducing the LV ejection fraction.<sup>1-5</sup> Recent clinical trials have shown that RVA pacing may induce heart failure, leading to hospitalization or heart failure-related death in patients with normal and depressed LV function.<sup>6-8</sup> On the other hand, LV ejection fraction has been shown to be closely related to LV twist.<sup>9</sup> RVA pacing impaired not only LV synchrony but also LV twist in a canine model with magnetic resonance imaging tagging.<sup>10</sup> We hypothesized that RVA pacing impairs the rotation of the LV apex and base and synchrony between LV apical and basal rotation, leading to a reduction in LV twist in the human heart.

Two-dimensional ultrasound speckle-tracking imaging, now widely available in clinical settings, can yield myocardial velocity with better temporal resolution than magnetic resonance imaging, and it has recently been shown to accurately measure LV twist.<sup>11</sup> The purpose of this study was to examine the impact of RVA pacing on LV rotational mechanics and the relation between the LV rotational parameters and the other dyssynchrony indexes.

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## METHODS

### Study Population

The study population consisted of 30 consecutive adult patients with sick sinus syndrome (mean age,  $74 \pm 4$  years) who had undergone the placement of transvenous permanent dual-chamber pacemakers for accepted indications: sinus node dysfunction occurring spontaneously or as a result of necessary drug therapy with documented symptomatic bradycardia or when a clear association between significant symptoms consistent with bradycardia and the actual presence of bradycardia was not documented. Right ventricular pacing leads were positioned at the right ventricular apex, and right atrial pacing leads were at the right atrial appendage. To be eligible to participate, patients had to have normal LV function without atrioventricular block. Exclusion criteria included ischemic heart disease, significant arrhythmia including advanced atrioventricular block, significant valvular heart disease, LV systolic dysfunction, hypertrophic cardiomyopathy, and prior coronary bypass or valve surgery. To exclude ischemic heart disease, all patients underwent coronary angiography before pacemaker implantation. In addition, we also evaluated 8 age-matched healthy volunteers in sinus rhythm as normal controls. The institutional clinical research and ethics committee approved this study. All patients provided written informed consent for the study.

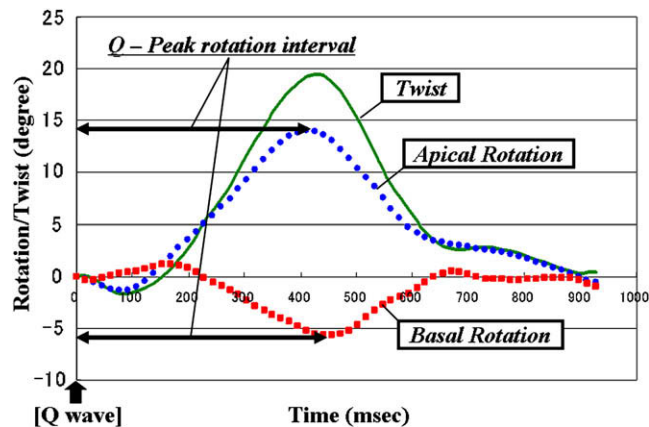
### Study Protocol

The study was designed to assess the acute effects on echocardiographic parameters, changing from intrinsic atrioventricular conduction to RVA pacing under electrocardiographic monitoring. Intrinsic atrioventricular conduction refers to AAI mode and RVA pacing to DDD mode. To ensure continuous RVA pacing in DDD mode, the atrioventricular delay was set at 20 ms shorter than that of intrinsic atrioventricular conduction. Initially, when pacemakers were programmed in AAI mode to retain intrinsic atrioventricular conduction, either with sinus rhythm or atrial pacing, echocardiographic evaluation was performed. Then, a few minutes after changing the pacemaker mode from AAI to DDD and confirming RVA pacing activation, the same echocardiographic parameters were evaluated. These echocardiographic evaluations were performed <1 week after pacemaker implantation.

### Echocardiography

Transthoracic echocardiography was performed in all patients in the left lateral decubitus position, using a commercially available system (Vivid 7; GE Healthcare, Milwaukee, WI). To minimize variability between examinations, all echocardiographic examinations were performed by 1 experienced echocardiographer. All images were recorded digitally and were analyzed offline using commercially available software (EchoPAC version 6.0; GE Healthcare). Images were obtained using an M3S probe in the parasternal (long-axis and short-axis) and apical (2-chamber and 4-chamber) views. In each plane, 3 consecutive cardiac cycles were acquired during a breath-hold period. LV end-diastolic and end-systolic volumes and LV ejection fraction were calculated from apical 2-chamber and 4-chamber images using the biplane Simpson's method.<sup>12</sup> For mitral inflow, the sample volume was placed at the mitral valve tips in the apical 4-chamber view. Mitral regurgitation was graded as follows: 1 = minimal (jet area/left atrial area < 10%), 2 = moderate (jet area/left atrial area, 10%-20%), 3 = moderate to severe (jet area/left atrial area, 20%-45%), and 4 = severe (jet area/left atrial area >45%).<sup>13</sup>

LV longitudinal dyssynchrony was assessed using color-coded Doppler tissue imaging. The frame rates ranged from 92 to 127



**Figure 1** Blue round and red square dots depict profile curves of LV apical and basal rotation. Counterclockwise rotation is represented by positive numbers. LV twist (green curved line) was calculated as the net difference between LV apical and basal rotation. The time from the Q wave to peak rotation (black arrow) was defined as the Q-peak rotation interval.

frames/s, depending on the sector width of the range of interest. To assess LV longitudinal dyssynchrony, the sample volume was placed in the basal portions of the septum and lateral wall; the time to peak systolic velocity was obtained in the septum and lateral wall, and the average of the septal-to-lateral delay in peak velocity in 3 cardiac cycles was calculated as LV longitudinal dyssynchrony.<sup>14</sup>

To assess LV radial dyssynchrony, we applied speckle tracking to the LV short-axis papillary muscle level and extracted 6 segmental time-strain curves. LV radial dyssynchrony was defined as the difference between the earliest and latest segments, as proposed by Suffoletto et al.<sup>15</sup>

We scanned apical and basal short-axis planes using a high frame rate (79 frames/s) and the second harmonic (1.7/3.4 MHz) for speckle-tracking imaging.<sup>11,16</sup> We obtained basal short-axis images at the mitral valve level and apical short-axis images at the level having LV cavity alone, with no visible papillary muscles.<sup>11,16</sup> The LV cross-section was made as circular as possible. We measured LV rotation using speckle-tracking imaging on the workstation. When echocardiographic image quality was unsuitable for quantitative speckle-tracking imaging analysis, we excluded the LV segments (7% of all LV segments). Plots of the basal and apical LV rotation speckle-tracking imaging data were exported to a spreadsheet program (Excel 2000; Microsoft Corporation, Redmond, WA) to calculate LV twist. LV twist was calculated as the net difference between LV apical and basal rotation (Figure 1). We also calculated LV untwisting velocity as LV relaxation function. Previous work with cardiac magnetic resonance in an animal model showed that LV untwisting velocity correlates closely with the time constant of LV relaxation.<sup>17</sup>

To assess the synchrony between LV apical and basal rotation, the interval from the beginning of the Q wave on the surface electrocardiogram to the peak rotation (Q-peak rotation interval) was obtained from the apical and basal short-axis images, and the difference between the apical and basal Q-peak rotation interval was calculated as an indicator of apical-basal rotation delay.

### Reproducibility

The reproducibility of measuring LV twist, apical Q-peak rotation interval, and basal Q-peak rotation interval was assessed by comparing measurements for different cardiac cycles in each patient. Subsequently, linear regression analysis and percentage absolute difference analysis were performed. Percentage absolute difference was

**Table 1** Baseline clinical characteristics and echocardiographic findings

Variables	Controls (n = 8)	Patients with SSS (n = 30)	P
Age (y)	65 ± 10	74 ± 7	NS
Men (%)	87.5	36.7	.01
QRS interval (ms)	105 ± 10	103 ± 9	NS
Echocardiographic parameters			
Ejection fraction (%)	67 ± 6	70 ± 7	NS
E/A ratio	1.3 ± 0.5	1.0 ± 0.4	NS
LVEDD (mm)	47 ± 4	49 ± 5	NS
Wall-thickness (mm)			
IVS	8.8 ± 1.0	8.5 ± 1.7	NS
PW	8.8 ± 1.0	8.5 ± 1.2	NS
Mitral regurgitation (grade)	0.5 ± 0.5	0.9 ± 0.8	NS
Dyssynchrony			
LV longitudinal dyssynchrony (ms)	12 ± 8	6 ± 9	NS
LV radial dyssynchrony (ms)	24 ± 15	39 ± 28	NS
Rotational measurements			
LV twist (°)	10.3 ± 9.0	16.5 ± 9.2	NS
Peak apical rotation (°)	8.2 ± 5.3	12.3 ± 7.0	NS
Peak basal rotation (°)	-4.5 ± 4.4	-5.3 ± 4.6	NS
Q-peak rotation interval (ms)			
Apex	386 ± 18	474 ± 165	NS
Base	376 ± 28	478 ± 191	NS
Apical-basal rotation delay (ms)	-10 ± 34	-7 ± 136	NS
LV untwisting velocity (°/s)	-109 ± 28	-113 ± 53	NS

IVS, Interventricular septum; LVEDD, LV end-diastolic diameter; PW, posterior wall; SSS, sick sinus syndrome. Data are expressed as mean ± SD.

**Table 2** Intraobserver variability for LV rotational measurements

Variable	Difference	Linear regression	
		r	P
LV twist (°)	9.4 ± 5.8	0.98	<.0001
Q-peak rotation interval (ms)			
Apex	11.6 ± 7.6	0.95	<.0001
Base	13.0 ± 9.3	0.97	<.0001

calculated by dividing the absolute difference of the two different cardiac cycles' values by their average value.

### Statistical Analysis

Data are reported as mean ± SD or as frequency (percentage). The *F* test was used to assess if measured data were distributed normally. In case of normally distributed data, the paired Student's *t* test was used for calculations. In case of a nonnormal distribution, Wilcoxon's signed rank test was performed. A *P* value < .05 was considered statistically significant. All calculations were performed using a commercially available statistical package (StatView version 5.0; SAS Institute Inc, Cary, NC).

## RESULTS

All patients completed the study protocol. Table 1 lists baseline characteristics of patients with sick sinus syndrome and healthy

**Table 3** Comparison between intrinsic atrioventricular conduction and RVA pacing

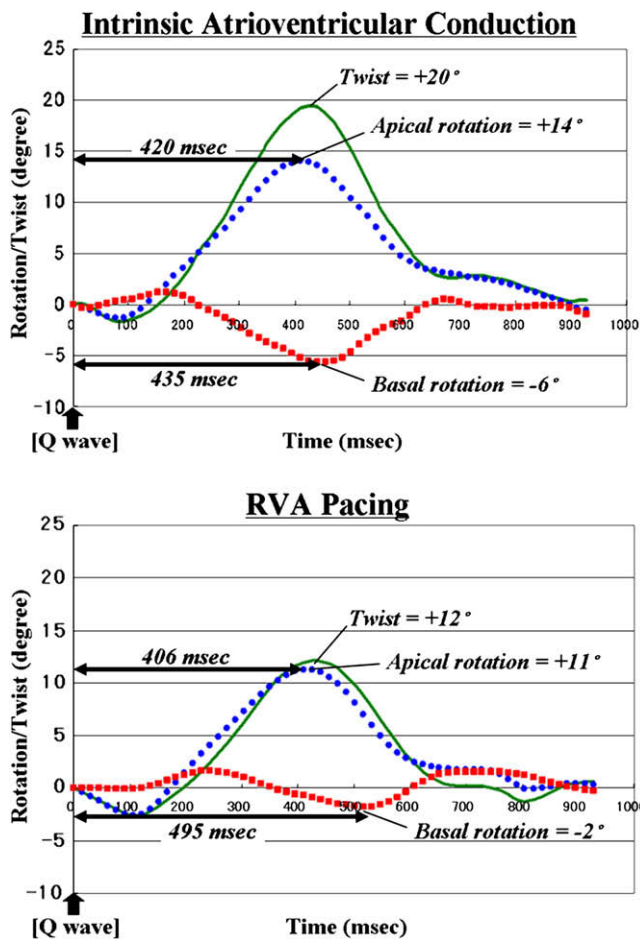
Variables	Controls	Intrinsic atrioventricular conduction	RVA pacing	P*
Heart rate during study (beats/min)	63 ± 10	61 ± 8	62 ± 4	NS
QRS interval (ms)	105 ± 10	103 ± 9	158 ± 47	.007
Ejection fraction (%)	67 ± 6	70 ± 7	65 ± 9	.0003
E/A ratio	1.3 ± 0.5	1.0 ± 0.4	1.1 ± 0.4	NS
Mitral regurgitation (grade)	0.5 ± 0.5	0.9 ± 0.8	0.9 ± 0.8	NS
Dyssynchrony				
LV longitudinal dyssynchrony (ms)	12 ± 8	6 ± 9	43 ± 32	<.0001
LV radial dyssynchrony (ms)	24 ± 15	39 ± 28	86 ± 70	<.0001
Rotational measurements				
LV twist (°)	10.3 ± 9.0	16.5 ± 9.2	10.3 ± 6.3	<.0001
Peak apical rotation (°)	8.2 ± 5.3	12.3 ± 7.0	8.4 ± 5.4	.007
Peak basal rotation (°)	-4.5 ± 4.4	-5.3 ± 4.6	-3.2 ± 3.4	.003
Q-peak rotation interval (ms)				
Apex	386 ± 18	474 ± 165	477 ± 191	NS
Base	376 ± 28	478 ± 191	565 ± 207	<.05
Apical-basal rotation delay (ms)	-10 ± 34	-7 ± 136	105 ± 162	.02
LV untwisting velocity (°/s)	-109 ± 28	-113 ± 53	-91 ± 39	.02

\*Intrinsic atrioventricular conduction versus RVA pacing.

volunteers. Baseline characteristics in patients with sick sinus syndrome did not significantly differ from those in healthy volunteers, except for sex (men with sick sinus syndrome 87.5% vs male controls 36.7%; *P* = .01). The reproducibility of measuring LV twist, apical Q-peak rotation interval, and basal Q-peak rotation interval is shown in Table 2.

### Acute Effects of Intrinsic Atrioventricular Conduction and RVA Pacing on LV Systolic and Diastolic Function, Synchrony, and Mitral Regurgitation

Differences between intrinsic atrioventricular conduction and RVA pacing with respect to LV systolic and diastolic function, synchrony, and mitral regurgitation are shown in Table 3. Immediately upon changing from intrinsic atrioventricular conduction to RVA pacing, LV ejection fraction was significantly reduced (*P* = .0003), while LV ejection fraction in both pacing modes was in the normal range (ejection fraction > 60%). LV longitudinal dyssynchrony was significantly longer with RVA pacing than with intrinsic atrioventricular conduction (43 ± 32 ms with RVA pacing vs 6 ± 9 ms with intrinsic atrioventricular conduction; *P* < .0001). LV radial dyssynchrony was also significantly longer with RVA pacing than with intrinsic atrioventricular conduction (86 ± 70 ms with RVA pacing vs 39 ± 28 ms with intrinsic atrioventricular conduction; *P* < .0001). These results indicated an amelioration of LV synchrony during RVA pacing. There was no change in E/A ratio or mitral regurgitation grade between intrinsic atrioventricular conduction and RVA pacing.



**Figure 2** Representative profile curves of LV rotation and twist in intrinsic atrioventricular conduction (top) and RVA pacing (bottom). Counterclockwise rotation is represented by positive numbers. LV twist (green curved line) was calculated as the net difference between LV apical and basal rotation. Black arrows indicate the Q-peak rotation interval.

**Acute Effects of Intrinsic Atrioventricular Conduction and RVA Pacing on LV Rotation, Twist, and Untwist**

Figure 2 shows representative profile curves of LV apical and basal rotation during intrinsic atrioventricular conduction and RVA pacing. By convention, counterclockwise rotation is represented by positive numbers. With both intrinsic atrioventricular conduction and RVA pacing, early systolic clockwise followed by counterclockwise rotation during systole was seen in the LV apex, and early systolic counterclockwise followed by clockwise rotation was seen in the LV base. However, in this representative case, both values of apical and basal rotation were lower during RVA pacing. Peak rotation decreased significantly in the LV apex ( $8.4 \pm 5.4^\circ$  with RVA pacing vs  $12.3 \pm 7.0^\circ$  with intrinsic atrioventricular conduction;  $P = .007$ ) and LV base ( $-3.2 \pm 3.4^\circ$  with RVA pacing vs  $-5.3 \pm 4.6^\circ$  with intrinsic atrioventricular conduction;  $P = .003$ ). Correspondingly, LV twist significantly decreased during RVA pacing ( $10.3 \pm 6.3^\circ$  with RVA pacing vs  $16.5 \pm 9.2^\circ$  with intrinsic atrioventricular conduction;  $P < .0001$ ). LV untwisting velocity was also lower during RVA pacing ( $-91^\circ/s \pm 39^\circ/s$  with RVA pacing vs  $-113 \pm 53^\circ/s$  with intrinsic atrioventricular conduction;  $P = .02$ ).

**Table 4** Correlations between rotational measurements and dyssynchrony indexes, ejection fraction, and QRS interval

Variables	Longitudinal dyssynchrony	Radial dyssynchrony	Ejection fraction	QRS interval
LV twist (°)	-0.30*	-0.36*	0.11	-0.16
Peak apical rotation (°)	-0.23	-0.27	0.13	-0.01
Peak basal rotation (°)	0.20	0.26	-0.11	0.19
Q-peak rotation interval (ms)				
Apex	-0.05	-0.23	-0.13	0.03
Base	0.30*	0.17	-0.18	0.21
Apical-basal rotation delay (ms)	0.43*	0.32	-0.08	0.25
LV untwisting velocity (°/s)	0.39*	0.42*	-0.27	0.18

\* $P < .05$ .

**Q-Peak Rotation Interval and Apical-Basal Rotation Delay**

There was no significant change in the Q-peak rotation interval between intrinsic atrioventricular conduction and RVA pacing in the LV apex (Table 3). However, in the LV base, the Q-peak rotation interval during RVA pacing was significantly longer than that during intrinsic atrioventricular conduction ( $565 \pm 207$  ms with RVA pacing vs  $478 \pm 191$  ms with intrinsic atrioventricular conduction;  $P < .05$ ). During intrinsic atrioventricular conduction, the LV apex and base rotated at almost the same time, whereas during RVA pacing, LV basal rotation was delayed compared with LV apical rotation. Consequently, apical-basal rotation delay during RVA pacing was significantly longer than during intrinsic atrioventricular conduction ( $105 \pm 162$  ms with RVA pacing vs  $-7 \pm 136$  ms with intrinsic atrioventricular conduction;  $P = .02$ ).

**Comparison of Rotational Parameters With Indexes of Dyssynchrony**

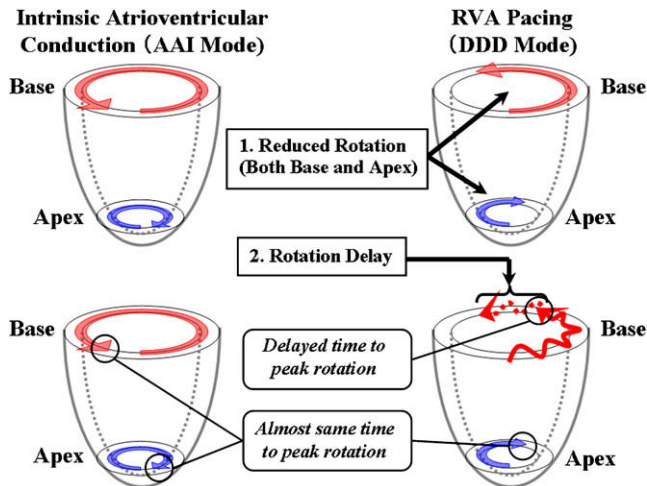
Among rotational parameters, LV twist and untwisting velocity were significantly correlated with LV longitudinal and radial dyssynchrony (Table 4). Basal Q-peak rotation interval and apical-basal rotation delay also had significant correlations with LV longitudinal dyssynchrony. None of the rotational parameters were correlated with LV ejection fraction or QRS intervals.

**DISCUSSION**

This study obtained echocardiographic information regarding the adverse effects of RVA pacing on LV rotation, twist, and untwist. First, RVA pacing impaired LV twist and untwist as well as LV synchrony in a human model. Second, RVA pacing decreased both apical and basal rotation and delayed basal rotation, resulting in LV apical-basal rotation delay. Decreases of both apical and basal rotation, and apical-basal rotation delay, might lead to LV twist impairment (Figure 3). Third, LV twist and untwisting velocity had significant correlations with LV longitudinal and radial dyssynchrony.

**LV Rotation, Twist, and Untwist During RVA Pacing**

RVA pacing has been reported to induce abnormal activation sequences and asynchronous patterns of LV contraction, especially between the LV septal and lateral walls, reducing the LV ejection



**Figure 3** Mechanism of impaired LV twist. RVA pacing decreased both apical and basal rotation and induced basal rotation delay, resulting in LV apical-basal rotation delay. Decreases in both apical and basal rotation, and apical-basal rotation delay, might lead to LV twist impairment.

fraction.<sup>1-5</sup> Several recent reports have highlighted the potential adverse effects of RVA pacing, showing that the incidence of symptomatic congestive heart failure increases in patients with RVA pacing.<sup>6,7,18,19</sup> On the other hand, LV rotation and twist also play an important role with respect to LV systolic function. This study demonstrated that RVA pacing decreased LV rotation, twist, and untwist, which might indicate impairment of LV systolic and relaxation function. RVA pacing also induced apical-basal rotation delay, possibly resulting in the impairment of LV twist. Although previous work has shown a significant correlation between LV twist and ejection fraction,<sup>20</sup> in this study, LV twist did not correlate with ejection fraction. The discrepancy might be caused by selection bias. The previous study included patients with LV systolic dysfunction,<sup>20</sup> whereas all patients of this study had normal LV systolic function.

#### LV Twist, Untwist, and Dyssynchrony During RVA Pacing

It is well known that RVA pacing induces dyssynchrony between the LV septal and lateral walls.<sup>21</sup> In the present study, we found that RVA pacing reduced LV twist and untwist, correlating with LV longitudinal and radial dyssynchrony. LV twist has the advantage of providing more global and thorough information on the left ventricle than LV longitudinal and radial dyssynchrony, because it integrates the apical mechanics that have far remained out of evaluation. Liu et al<sup>22</sup> demonstrated that the dyssynchrony during RVA pacing could be assessed by time-volume analysis for the global 17 segments of the left ventricle with 3-dimensional echocardiography, not by Doppler tissue imaging analysis for 12 nonapical segments with 2-dimensional echocardiography. LV apical mechanics could affect LV dyssynchrony during RVA pacing. Sade et al<sup>23</sup> reported that LV twist had the highest sensitivity and specificity to predict cardiac resynchronization therapy response among all other parameters, including radial and longitudinal dyssynchrony. We assume that LV twist may potentially be an additional method to longitudinal and radial LV dyssynchrony information in the evaluation of RVA-paced candidates for upgrading to cardiac resynchronization therapy. Eldadah et al<sup>21</sup> showed the benefit of upgrading chronically RVA-paced heart failure patients to cardiac

resynchronization therapy, by positioning the LV lead in a basal to midposterolateral branch vein of the coronary sinus. The beneficial effects of dual-site right ventricular pacing (right ventricular outflow plus RVA) in a small group of patients in whom coronary sinus lead implantation failed because of technical difficulties during cardiac resynchronization therapy has been reported.<sup>24</sup> Pacing in a basal to midposterolateral branch vein of the coronary sinus or right ventricular outflow might reduce apical-basal rotation delay.

#### Study Limitations

First, we tested the different pacing modes only in the acute setting. Hence, the chronic effects on LV performance could not be predicted by our study. Second, although setting the atrioventricular delay 20 ms shorter than intrinsic atrioventricular conduction made it possible to change from AAI to DDD mode, the detrimental effects of a sub-optimal atrioventricular interval on cardiac output in a small group of patients have been reported.<sup>25</sup> Slight shortening of the atrioventricular interval could affect the LV inflow pattern, possibly leading to the impairment of LV rotation and twist. Third, although mitral regurgitation jet area was used for the quantification of mitral regurgitation in this study, additional methods, such as vena contracta and proximal isovelocity surface area, might make its evaluation more accurate.<sup>26</sup>

#### Clinical Implications and Conclusions

Our data demonstrate that RVA pacing decreased LV rotation, twist, and untwist and induced LV apical-basal rotation delay. Depending on our results, in the acute phase, AAI mode seems to be the superior pacing mode for LV twist and untwist, as well as for other dyssynchrony indexes. Research on LV twist, untwist, and apical-basal rotation delay in RVA-paced heart failure patients upgraded to cardiac resynchronization therapy may help assess the effectiveness of cardiac resynchronization therapy. However, long-term clinical follow-up trials of RVA-paced or cardiac resynchronization therapy patients are needed to assess the clinical applications of LV twist and untwist.

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