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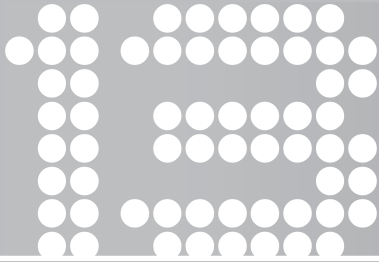Tops, L.F.

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Acute effects of right ventricular apical pacing on left ventricular synchrony and mechanics

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ABSTRACT

Background: Long-term right ventricular (RV) apical pacing has a detrimental effect on left ventricular (LV) function. However, the acute effects of RV apical pacing on LV mechanics remain unclear. The purpose of this study was to assess the acute impact of RV apical pacing on global LV function, evaluating LV contraction synchrony and LV shortening and twist, using 2-dimensional (2D) speckle-tracking strain imaging.

Methods and Results: A group of 25 patients with structural normal hearts referred for electrophysiological (EP) study were studied. Two-dimensional echocardiography was performed at baseline and during RV apical pacing at the time of the EP study. Changes in LV synchrony and mechanics (longitudinal shortening and twist) were assessed using speckle-tracking strain imaging. In addition, 25 controls matched by age, gender and LV function were studied during sinus rhythm. The group of patients (44±12 years, 10 men) and the group of controls (48 ± 3 years, 8 men) showed comparable LV synchrony, LV longitudinal shortening and LV twist at baseline. However, during RV apical pacing, a more dyssynchronous LV contraction was observed in the patients (from 21 ms [Q_1:10, Q_3:53] to 91 ms [Q_1:40, Q_3:204], p<0.001) together with an impairment in LV longitudinal shortening (from -18.3 ± 3.5% to -11.8 ± 3.6%, p<0.001) and in LV twist (from 12.4 ± 3.7º to 9.7 ± 2.6º, p=0.001).

Conclusions: During RV apical pacing, an acute induction of LV dyssynchrony is observed. In addition, LV longitudinal shortening and LV twist are acutely impaired.

INTRODUCTION

Several animal and human studies have demonstrated detrimental effects of right ventricular (RV) apical pacing on cardiac function (1-4). The direct electrical stimulation of the RV apex induces an abnormal activation sequence and asynchronous ventricular contraction (3-5). Subsequently, left ventricular (LV) performance is impaired with a decrease in stroke volume and an abnormal LV relaxation (2). In patients with severe LV dysfunction, these effects are more pronounced and permanent RV apical pacing may result in a higher risk of morbidity and mortality at long-term follow-up (6,7). Recently, it has been shown that patients with long-term RV pacing and LV dysfunction also had LV dyssynchrony (8,9). The question that arises from this observation is whether RV pacing induced LV dyssynchrony resulted in LV dysfunction with heart failure, or whether RV pacing resulted in LV dysfunction and heart failure with subsequent development of LV dyssynchrony.

Importantly, in the majority of the studies that thus far have evaluated the long-term effects of RV apical pacing, the study population comprised patients with structural heart disease, which is a confounding factor that may amplify the detrimental effects of RV pacing on LV function (6,10,11). The exact effects of RV apical pacing on LV function in patients without structural heart disease have not been studied extensively (12). In addition, primarily the long-term effects of RV apical pacing have been studied, and not much information is available on the acute effects of RV pacing on LV function and LV dyssynchrony.

The recently introduced echocardiographic speckle-tracking analysis enables comprehensive evaluation of LV mechanics (LV synchrony, LV systolic function and LV twist) by studying LV deformation in 3 directions (radial, longitudinal and circumferential) (13-16). Importantly, this technique may reveal more subtle changes in LV systolic function, as compared to conventional measures such as LV ejection fraction.

Accordingly, the purpose of the present study was to assess the acute impact of RV apical pacing on global LV function in a group of patients without structural heart disease, evaluating LV contraction synchrony and LV global longitudinal shortening and twist, using 2-dimensional (2D) speckle-tracking strain imaging.

METHODS

Study population

Twenty-five patients, who were referred for an electrophysiological (EP) study for evaluation of supraventricular arrhythmias, were included in the present study. Inclusion criteria were: age>18 years old, no evidence of structural heart disease by 2D echocardiography, QRS duration on surface electrocardiogram <120 ms and New York Heart Association functional class I.

Study protocol

In the patient group, echocardiography was performed during sinus rhythm before the EP study, and during RV apical pacing at the end of the EP study. During the EP study, a standard diagnostic catheter (6F, Quadripolar catheter, Biosense-Webster, Diamond Bar, CA, USA) allowing temporary pacing was positioned in the RV apex. Constant RV apical overdrive pacing was performed for 5 minutes. To ensure continuous capture, RV apical pacing was performed with a cycle length of at least 100 ms shorter than the baseline cycle length. After 5 minutes, the echocardiogram was acquired during RV apical pacing. Surface electrocardiograms were recorded during sinus rhythm and RV pacing.

In addition, 25 controls frequency-matched for age, gender, body surface area and LV systolic function were selected from an echocardiographic database. The control group comprised patients referred for echocardiography with atypical chest pain, palpitations or syncope without murmur. In particular, only patients with normal LV systolic function without LV dilatation were selected. Furthermore, subjects who were referred for echocardiographic evaluation of known valvular disease, murmur, or heart failure were excluded.

Therefore, all subjects (both patients and controls), had normal echocardiograms, without structural heart disease. Patients underwent 2D echocardiography during sinus rhythm and during RV apical pacing (at the EP laboratory) whereas controls were imaged at the echocardiography laboratory during sinus rhythm only. Informed consent to participate was obtained from all subjects.

Echocardiography

A commercially available system was used (Vingmed Vivid 7 or Vivid-I, General Electric-Vingmed, Milwaukee, Wisconsin) and data were obtained using a 3.5-MHz transducer at a depth of 16 cm in the parasternal (long- and short-axis) and apical (2-, 3- and 4-chamber) views. Data acquisition was performed by an experienced sonographer during sinus rhythm and RV apical pacing with the patients in the supine position. Special care was taken to avoid either oblique parasternal short-axis views of the LV or foreshortened LV apical views.

Acquired data were transferred to an off-line workstation for further analysis (EchoPac version 6.0.1, General Electric-Vingmed). Left ventricular dimensions (end-diastolic and end-systolic diameter, septum and posterior wall thickness) were measured from the M-mode recordings derived from parasternal long-axis views. Furthermore, LV volumes and LV ejection fraction were measured from the 2- and 4-chamber apical views using the biplane Simpson's rule (17).

Speckle-tracking strain analysis

From standard gray-scale images, 2D speckle-tracking strain analysis was performed to study several aspects of LV mechanics: LV synchrony, global longitudinal shortening and LV twist. For this purpose, novel speckle-tracking software was used, as previously described (16). In

brief, this technique allows angle-independent measurement of myocardial strain in 3 different directions: circumferential shortening and radial thickening in the short-axis views and longitudinal shortening in the apical views. Natural acoustic markers (or speckles), equally distributed in the myocardial wall, form a characteristic pattern that is tracked from frame-to-frame along the cardiac cycle. The change in the position of the speckle pattern with respect to the initial position is used to calculate myocardial strain (16). In the selected views, the endocardial border is traced manually at an end-systolic frame. Next, a region of interest, that includes the myocardial wall, is displayed automatically. The software allows for further adjustment of the region of interest in order to fit the entire myocardial wall within the boundaries. Then, the tracking quality can be evaluated and validated. Finally, the region of interest is divided in 6 segments and the time-strain curves along the cardiac cycle for each segment are displayed.

LV synchrony To evaluate LV synchrony, mid ventricular short-axis images at the level of the papillary muscles were selected and 2D speckle-tracking radial strain analysis was performed, as previously described (15). The time from the onset of QRS to the peak strain value was measured for each segment (anteroseptal, anterior, lateral, posterior, inferior and septal). Subsequently, the difference between the earliest and the latest segments was calculated. LV dyssynchrony was defined as a time difference ≥130 ms between the earliest and the latest segments, as previously described (5,15). To compare differences between sinus rhythm and RV apical pacing, LV dyssynchrony was normalized to RR interval, as previously described (18).

LV longitudinal shortening In addition to conventional measurements of LV systolic function based on 2D echocardiography, LV longitudinal shortening was evaluated. For this purpose, automated function imaging, a method based on 2D speckle-tracking strain imaging, was used (16). The selected views were the apical 2-, 3- and 4-chamber views. In brief, from an end-systolic frame of each view, 2 basal points at the mitral annulus, and 1 point at the apex, were used as reference points to trace the region of interest spanning the entire myocardial wall. Using a 17-segment model, the peak systolic longitudinal strain for each LV segment was calculated and presented as a "polar map", with the average value of peak systolic longitudinal strain for each view and the averaged global longitudinal peak systolic strain for the complete LV (Figure 1). Conventionally, longitudinal shortening is presented in negative values.

LV twist The helical disposition of the myocardial fibers determines the characteristic wringing motion of the LV. As previously described, viewed from the LV apex, the apical segments of the LV show a systolic counter-clockwise rotation whereas the basal segments of the LV show a clockwise rotation (19). The assessment of LV rotation by 2D speckle-tracking strain imaging requires the acquisition of the LV short-axis at the apical level (the most distal level from the papillary muscles) and at the basal level (the level where the leaflets of the mitral valve are visualized) (14). In each short-axis image, the region of interest including the entire myocardial wall
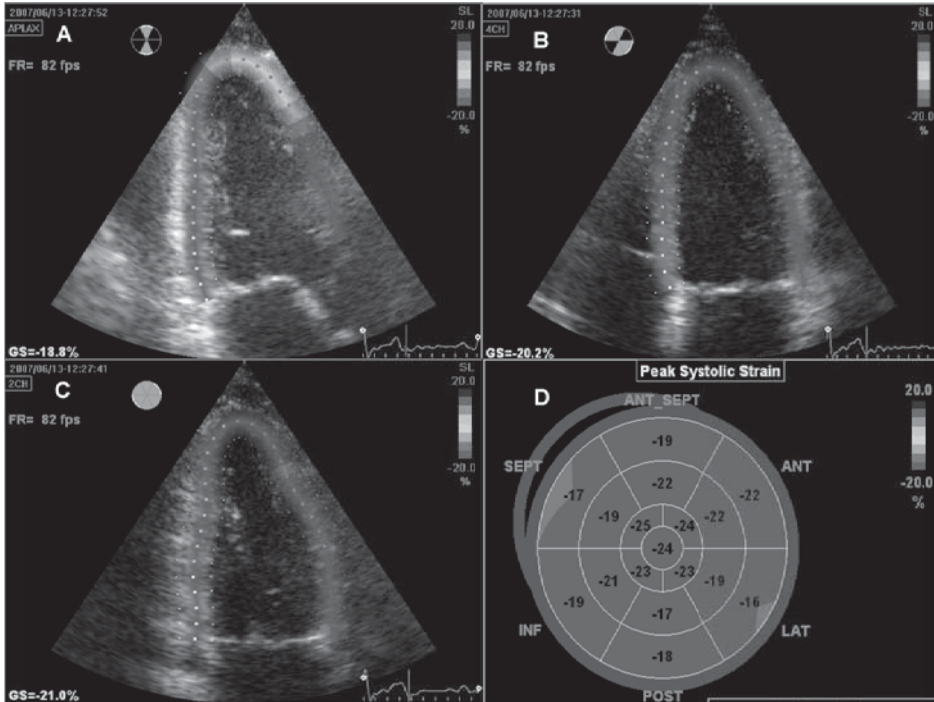
Figure 1. The automated function imaging algorithm enables the measurement of global LV longitudinal strain from 3 standard apical views of the LV. The apical long-axis view of the LV (panel A) should be measured first, defining the aortic valve closure. The time interval between the R wave and the aortic valve closure is used as a reference for the measurement of LV shortening at 4- and 2-chamber view loops (panels B and C respectively). Finally, the algorithm provides the peak systolic longitudinal strain for each LV segment in a "bull's eye" plot, with the average value of peak systolic longitudinal strain for each view and the averaged global longitudinal peak systolic strain for the complete LV (panel D).

is traced at an end-systolic frame and divided into 6 segments. Subsequently, the time-rotation curves are displayed along the cardiac cycle. The counter-clockwise rotation is conventionally presented as positive values and the clockwise rotation as negative values. The difference between the systolic apical and basal rotation results in LV twist (Figure 2)(14).

Reproducibility of the assessment of LV rotation was analyzed with repeated measurements by an experienced observer at two different time points and by a second experienced observer. Intra- and inter-observer agreements for these measurements were evaluated by Bland-Altman analysis. Intra-observer variability was good, with an excellent agreement (mean ± 2SD was -0.1 ± 2.2º) between two repeated measurements. Similarly, inter-observer variability showed an excellent agreement (mean ± 2SD was 0.14 ± 3.4º).

Statistical analysis

All variables were normally distributed (as assessed by Kolmogorv-Smirnov test), except LV dyssynchrony indexed to RR interval. Continuous variables are presented as mean ± SD, when normally distributed, and as median (25th and 75th percentiles: Q_1, Q_3) when non-normally distributed. Comparisons between the patients and the matched controls were performed
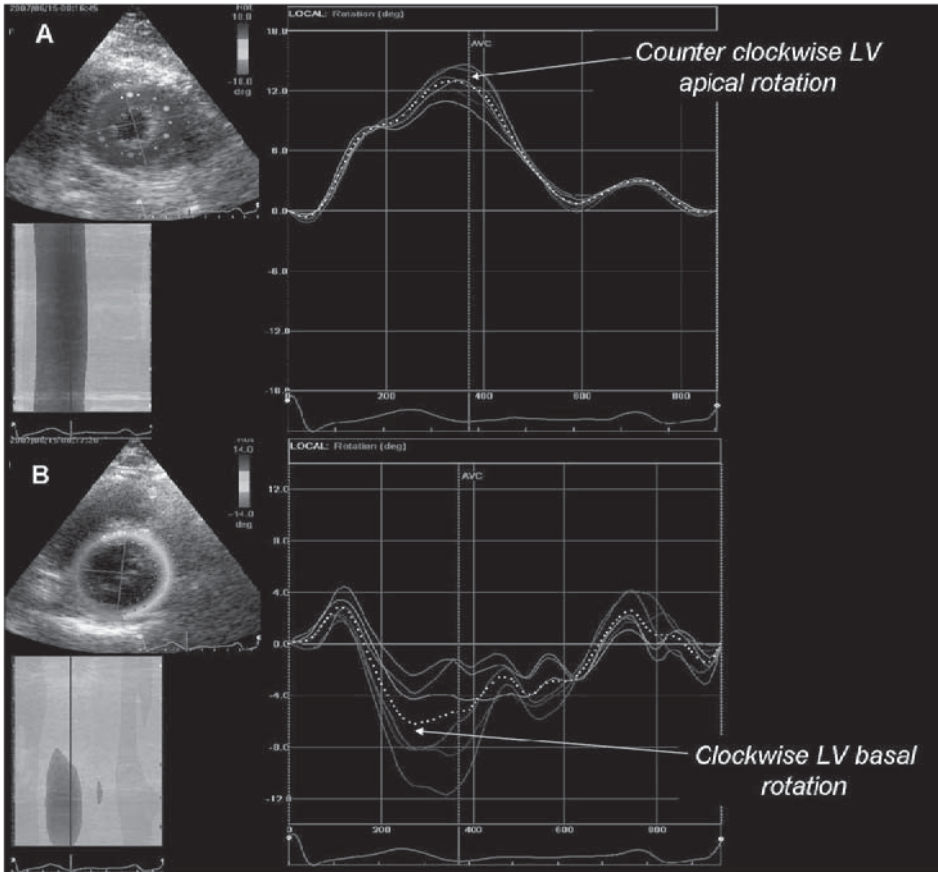
Figure 2. Assessment of LV twist by 2D speckle-tracking strain imaging. LV twist was calculated using 2D speckle-tracking strain imaging applied to LV apical (panel A) and basal (panel B) short-axis view. The LV apex demonstrates a counter clockwise systolic peak rotation, whereas the LV base shows a clockwise systolic peak rotation. The difference between the apical and the basal systolic peak rotation results in LV twist.

using the unpaired Student t-test (for normally distributed variables) and Mann-Whitney U-test (for non-normally distributed variables). Comparisons within the group of patients during sinus rhythm and RV apical pacing were performed using the paired Student t-test (for normally distributed variables) and Wilcoxon Signed Ranks test (for non-normally distributed variables). All statistical analyses were performed with SPSS software (version 16.0, SPSS Inc., Chicago, Illinois). All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

RESULTS

The study protocol could be completed in all 25 patients (mean age 44 ± 12 years, 10 men/15 women). In 15 (60%) patients, atrioventricular nodal reentry tachycardia was demonstrated

during the EP study, whereas in the remaining 10 patients, no tachyarrhythmia was documented. In all individuals, echocardiographic image quality was sufficient for quantitative analysis. Echocardiographic data acquisition was performed at a mean frame rate of 84 ± 13 frames/sec. By definition, at baseline all the patients and matched controls showed structural normal hearts with synchronous LV systolic contraction as evaluated by 2D speckle-tracking radial strain imaging.

To acquire the echocardiographic data during RV apical pacing, continuous capture was ensured by pacing with a cycle length of at least 100 ms shorter than the baseline cycle length. Mean heart rate was 69 ± 14 bpm at baseline and 106 ± 11 bpm during RV apical pacing (p<0.001). During RV apical pacing, the QRS duration on the surface electrocardiogram was significantly longer as compared to baseline (131 ± 18 ms vs. 92 ± 7 ms; p=0.001).

Effects of RV apical pacing on LV dimensions and volumes

Baseline LV dimensions and volumes were comparable between the patients and the matched controls (Table 1). During RV apical pacing, a significant decrease in LV end-diastolic diameter and volume were observed in the patients, whereas LV end-systolic diameter and volume did not change (Table 2). Consequently, LV ejection fraction decreased significantly from 56 ± 8% to 48 ± 9% (p=0.001).

Effect of RV apical pacing on LV mechanics

LV synchrony With the use of 2D speckle-tracking radial strain, LV synchrony was assessed in the study population. Median time difference between the earliest and latest segments (corrected by RR interval) was similar in the patient group and the matched controls at baseline (Table

Table 1. Echocardiographic characteristics of the study population

	Patients (n=25)	Controls (n=25)	p-value
Age, yrs	44 ± 12	48 ± 3	0.100
Gender, M/F	10/15	8/17	0.556
Heart rate, bpm	69 ± 14	72 ± 12	0.469
LV dimensions and volumes			
LV end-diastolic diameter (mm)	49 ± 5	49 ± 4	0.567
LV end-systolic diameter (mm)	30 ± 5	27 ± 4	0.126
Interventricular septum thickness (mm)	10 ± 2	10 ± 2	0.816
Posterior wall thickness (mm)	10 ± 2	10 ± 2	0.787
LV end-diastolic volume (ml)	99 ± 26	95 ± 22	0.538
LV end-systolic volume (ml)	44 ± 16	38 ± 11	0.183
LV ejection fraction (%)	56 ± 8	60 ± 6	0.069
LV mechanics			
LV synchrony (RR-indexed) (ms) *	21 (10, 53)	20 (0, 68)	0.953
LV longitudinal shortening (%)	-18.3 ± 3.5	-18.5 ± 4.1	0.947
LV apical rotation (º)	7.1 ± 3.5	6.4 ± 3.5	0.507
LV basal rotation (º)	-5.4 ± 2.7	-6.6 ± 2.4	0.084
LV twist (º)	12.4 ± 3.7	13.0 ± 3.2	0.538

*expressed as median (25th, 75th percentiles); LV = left ventricular.

Table 2. Changes in LV dimensions, volumes and mechanics during RV apical pacing in the 25 patients undergoing electrophysiological testing

	Sinus Rhythm	RV apical pacing	Difference (RV-SR)	p-value (RV vs. SR)
LV dimensions and function				
LV end-diastolic diameter (mm)	49 ± 5	45 ± 6	-4.0 ± 5.2	<0.001
LV end-systolic diameter (mm)	30 ± 5	29 ± 6	-0.2 ± 4.5	0.827
LV end-diastolic volume (ml)	99 ± 26	88 ± 25	-11.0 ± 12.2	<0.001
LV end-systolic volume (ml)	44 ± 16	45 ± 16	1.0 ± 11.4	0.615
LV ejection fraction (%)	56 ± 8	48 ± 9	-8.0 ± 10.2	0.001
LV mechanics				
LV synchrony (RR-indexed) (ms)*	21 (10, 53)	91 (40, 204)	50 (12,174)	<0.001
LV longitudinal shortening (%)	-18.3 ± 3.5	-11.8 ± 3.6	7.0 ± 4.0	<0.001
LV apical rotation (º)	7.1 ± 3.5	6.7 ± 2.6	-0.4 ± 3.2	0.573
LV basal rotation (º)	-5.4 ± 2.7	-3.0 ± 2.1	2.4 ± 2.8	<0.001
LV twist (º)	12.4 ± 3.7	9.7 ± 2.6	-2.7 ± 3.6	0.001

*expressed as median (25th, 75th percentiles); LV= left ventricular; RV= right ventricular; SR= sinus rhythm.

1). In contrast, during RV apical pacing, the time difference between the earliest and the latest segments increased significantly from 21 ms (Q_1: 10, Q_3: 53) to 91 ms (Q_1: 40, Q_3: 204) (p<0.001). In 9 (36%) patients, a time difference >130 ms between the earliest and the latest activated segments was present during RV apical pacing, indicating the presence of LV dyssynchrony. An example of a patient with LV dyssynchrony during RV pacing is shown in Figure 3.

LV longitudinal shortening At baseline, the LV longitudinal shortening assessed by automated function imaging was comparable between patients and matched controls. Mean peak systolic global longitudinal strain was -18.3 ± 3.5% in the patients and -18.5 ± 4.1% in the matched controls (p=0.9). However, the LV global longitudinal strain value decreased significantly during RV apical pacing from -18.3 ± 3.5% to -11.8 ± 3.6% (p<0.001). Representative examples of LV longitudinal shortening during sinus rhythm and RV pacing are shown in Figure 4.

LV twist At baseline, no significant differences in LV rotation and twist between the patients and matched controls were observed (Table 1). However, during RV apical pacing, LV rotation showed significant changes. While the LV apex showed a slight decrease in rotation (from 7.1 ± 3.5º to 6.7 ± 2.6º, p=0.6), the base of the LV showed a significant decrease in rotation (from -5.4 ± 2.7º to -3.0 ± 2.1º, p<0.001). Consequently, LV twist was significantly impaired during RV apical pacing (from 12.4 ± 3.7º to 9.7 ± 2.6º, p=0.001). An example of a patient with a significant decrease in LV twist during RV pacing is shown in Figure 5.
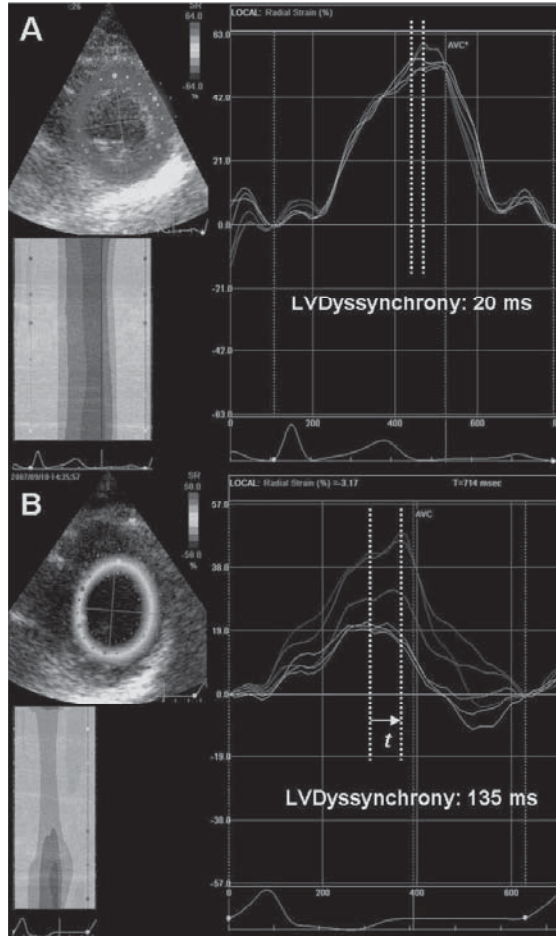
Figure 3. Changes in LV synchrony during RV apical pacing. LV dyssynchrony was measured using 2D speckle-tracking radial strain applied to midventricular short-axis images. A synchronous contraction was observed in sinus rhythm (panel A). During RV apical pacing, the time delay between the earliest and latest segments increased significantly, showing a more dyssynchronous LV contraction (panel B).

DISCUSSION

The present study provides more insight into the acute effects of RV apical pacing on cardiac mechanics in patients with structural normal hearts. Right ventricular apical pacing acutely induced dyssynchronous LV contraction associated with impairment in LV longitudinal systolic function. Furthermore, a deleterious effect on the characteristic torsional deformation of the LV during systole was noted.

Changes in LV dimensions induced by RV apical pacing
The baseline LV dimensions observed in the present study were comparable in patients and controls. However, during RV apical pacing a decrease in LV end-diastolic diameter and volume
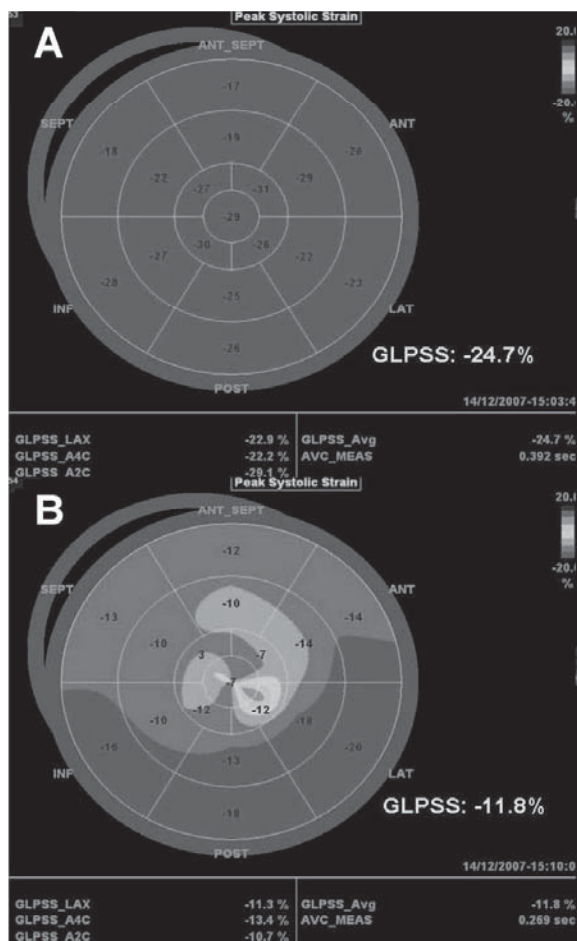
Figure 4. This figure shows the changes in global longitudinal peak systolic strain (GLPSS) in the same patient as in Figure 2. The LV longitudinal shortening was assessed on standard apical views using automated function imaging. Panel A shows the polar map with a normal and homogeneous GLPSS during sinus rhythm. However, during RV apical pacing, a significant decrease in GLPSS was observed (panel B).

was observed, whereas the LV end-systolic dimensions remained unchanged. Consequently, LV ejection fraction showed a significant impairment during RV pacing.

In general, information on the acute effects of RV apical pacing on LV dimensions and volumes in patients with preserved LV function is scarce (2,10). Recently, Liu et al. studied the acute effects of RV apical pacing on LV function in a group of 35 patients with sick sinus syndrome using real-time 3-dimensional echocardiography (10). During RV apical pacing, patients showed a decrease in LV end-diastolic volume (from 79 ± 22 ml to 76 ± 20 ml, p=0.07) and in LV ejection fraction (from $57 \pm 8\%$ to $54 \pm 8\%$, p=0.01) (10). In addition, in a group of patients with preserved LV ejection fraction studied by Lieberman et al. RV apical pacing induced a moderate decrease in LV ejection fraction (from $51 \pm 12\%$ to $48 \pm 14\%$, p=NS) whereas the LV dimensions remained unchanged (2).
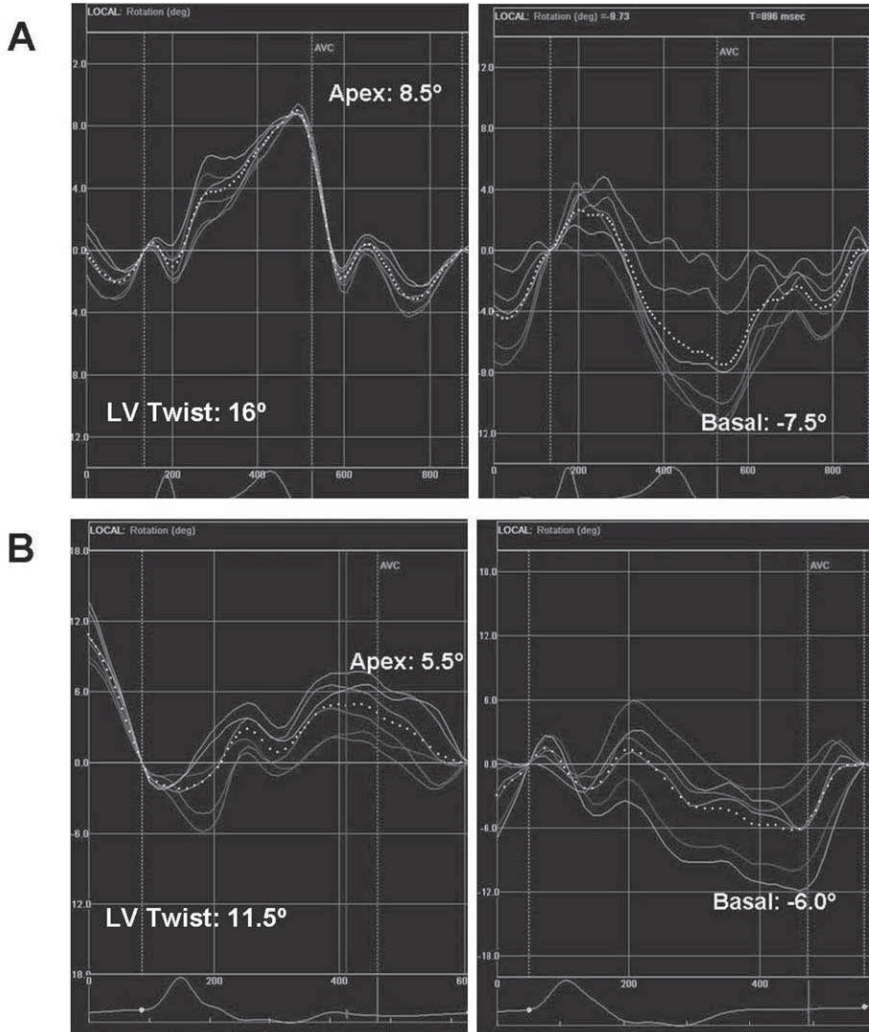
Figure 5. Changes in left ventricular (LV) rotation during RV apical pacing. LV rotation was assessed by applying 2D speckle-tracking strain imaging at the LV apex and base. Subsequently, LV twist is derived from the difference between the apical and basal rotations. This figure demonstrates LV rotation and twist in the same patient as in Figure 3 and 4. Panel A shows both apical and basal LV rotations during sinus rhythm. During RV apical pacing (panel B), a decrease in both apical and basal LV rotations was observed, with a subsequent significant decrease in LV twist.

Several factors may contribute to the decrease in LV end-diastolic dimension and volume and LV ejection fraction during RV apical pacing. Normal LV diastolic filling may be impaired by the loss of normal atrioventricular conduction and subsequent decrease in left atrial contribution to diastolic filling (20,21). In addition, the earlier activation of the RV may hamper LV filling that is accomplished by the shared interventricular septum (20-22). Both mechanisms may result in a decrease in LV pre-load during RV apical pacing and, according to the Frank-Starling law, result in a lower LV stroke volume.

Changes in LV synchrony during RV apical pacing

In the present study, the synchronicity of the LV was evaluated by 2D speckle-tracking radial strain imaging, measuring the time difference between the earliest and the latest activated segments. Using this technique, synchronous contraction of the LV was observed in both the controls and the patients at baseline. During RV apical pacing, the time difference between the earliest and the latest activated segments increased significantly, reflecting a more dyssynchronous contraction pattern of the LV. In particular, 9 (36%) patients exhibited significant LV dyssynchrony (>130 ms between the earliest and the latest activated segments) during RV pacing.

Several animal and human studies have reported the acute effects of RV apical pacing on LV synchrony (10,12,23). Wymann et al. demonstrated the changes in LV mechanical activation synchrony during RV apical pacing using tagged-magnetic resonance imaging in an experimental study (23). During RV apical pacing, the breakthrough of the mechanical activation was located at the interventricular septum and spread along the LV walls ending at the lateral wall (23). As a result, the mechanical activation delay was significantly higher during RV apical pacing (77.6 ± 16.4 ms) as compared to right atrial pacing (43.6 ± 17.1 ms).

Similarly, clinical studies have observed an acute induction of LV systolic dyssynchrony by RV apical pacing (10,12). Fornwalt et al. assessed the effects of RV apical pacing on systolic dyssynchrony using tissue Doppler imaging in 14 pediatric patients with normal cardiac structure and function (12). After 1 minute of RV apical pacing significant LV systolic dyssynchrony was noted, compared with sinus rhythm (from 49 ± 28 ms to 94 ± 47 ms, p<0.05). In addition, Liu et al. demonstrated an acute increase of LV systolic dyssynchrony index assessed with real-time 3-dimensional echocardiography during RV apical pacing in a group of patients with sick sinus syndrome (from 5.3 ± 2.1% to 7.0 ± 2.5%) (10).

The induction of LV dyssynchrony by RV apical pacing, as observed in the present and previous studies may be explained by changes in the electro-mechanical activation pattern during pacing. During ectopic activation of the LV by RV apical pacing, the depolarization impulse spreads through the slower-conducting myocardium rather than through the His-Purkinje system, resulting in a heterogeneous electrical and mechanical activation of the LV (24). However, it remains undetermined why some patients develop LV dyssynchrony during RV pacing while other patients do not.

Changes in LV shortening and twist induced by RV apical pacing

In the present study, changes in LV systolic mechanics were evaluated, focusing on LV longitudinal shortening and LV twist. In sinus rhythm, patients and controls showed comparable values of LV shortening and LV twist. However, during RV apical pacing, a significant decrease in both parameters was observed. The complex architecture of the LV determines a characteristic deformation pattern consisting of systolic shortening in the longitudinal and circumferential directions together with thickening in the radial direction (25). When viewed from the LV apex, this deformation pattern results in a typical wringing movement with a net counter-clockwise

rotation of the apex relative to the base of the heart (14). Any abnormality in this complex pattern of deformation and twist could significantly affect cardiac performance.

Several experimental studies have demonstrated changes in LV strain during RV pacing (3,23,25,26). Prinzen et al. described the non-uniformity of myocardial fiber strain during RV pacing as compared to the uniformity observed during right atrial pacing using sonomicrometry technique in a dog-model (3). Interestingly, in the early-activated LV areas the amount of shortening was lower than in the remote areas, resulting in a decrease in the net LV strain pattern during RV pacing (3). In addition, Liakopoulos et al. evaluated the effects of RV apical pacing on LV segmental shortening in a swine-model with sonomicrometry technique as well (25). The authors observed a pronounced decrease in LV segmental shortening during RV apical pacing at the posterior wall (from $18.8 \pm 6.1\%$ in sinus rhythm to $13.6 \pm 9.6\%$ during RV apical pacing, $p<0.05$) (25).

In the present study, the novel automated function imaging algorithm was used to assess global LV systolic shortening. Similar to the aforementioned studies, a significant decrease in LV longitudinal shortening was observed acutely during RV apical pacing. In addition, the resultant torsional movement of the LV showed a significant decrease during RV apical pacing. A decrease in both apical and basal rotation was observed during RV pacing in the present study. However, this decrease was more pronounced in the LV basal level.

A reduction in LV strain and LV twist has been previously reported in several clinical situations (hypertrophic cardiomyopathy, aortic stenosis and myocardial infarction) (27-29). However, the effect of RV apical pacing on LV twist has only been studied in animal experiments (30,31). Buchalter et al. demonstrated that the LV torsional movement depends on the sequence of LV depolarization, showing significant reduction in the LV twist during RV apical pacing (30). Furthermore, Sorger et al., in a tagged magnetic resonance study, observed a dramatic decrease in LV twist during RV apical pacing as compared to atrial pacing ($6.1 \pm 1.7°$ vs. $11.1 \pm 3.5°$, $p<0.001$) (31). The results of the current study are in agreement with these previous studies. Moreover, the present findings illustrate that the decrease in LV twist is simultaneous to the impairment in LV longitudinal shortening. The long-term effects of RV apical pacing on LV strain and twist however are still unclear and need further study.

Clinical implications

Previous studies demonstrated that long-term RV apical pacing may increase the risk of LV dysfunction and heart failure associated with the presence of LV dyssynchrony by 25-30% (9,32). The precise time course of development of these phenomena (LV dysfunction, heart failure and LV dyssynchrony) after RV pacing is currently unclear. In the present study, 36% of the patients developed significant LV dyssynchrony acutely during RV apical pacing, as assessed by 2-dimensional speckle-tracking strain imaging. In addition, significant impairment in LV systolic function was observed reflected by reduced LV ejection fraction, but also an impaired LV

longitudinal shortening and reduced LV twist. Whether this acutely induced LV dyssynchrony is the basis for the development of heart failure after long-term RV pacing needs further study.

Study Limitations

Some limitations need to be addressed. First, short-term effects of RV apical pacing on LV mechanics were assessed in the present study and, to avoid intrinsic ventricular conduction, pacing rate was set to 25% over the normal sinus rhythm, resulting in a high heart rate. These non-physiological conditions may preclude us to draw conclusions about the long-term effects of chronic RV pacing on LV performance. Second, all patients were considered to have structural normal hearts according to the clinical history, physical examination and the results of the complementary diagnostic exams performed. Unfortunately, endomyocardial biopsies were not available to confirm the absence of structural heart disease. Finally, additional studies evaluating different pacing sites and longer follow-up are needed to better understand the long-term effects of the acutely induced changes in LV mechanics by RV pacing.

CONCLUSIONS

In the present study, speckle-tracking analysis applied to conventional 2D echocardiography was used to study the acute effects of RV apical pacing on LV mechanics. Right ventricular apical pacing acutely induced a dyssynchronous LV contraction together with a decrease LV longitudinal function. In addition, the characteristic torsional deformation of the LV during systole was impaired acutely by RV apical pacing.

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