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IMPACT OF RIGHT VENTRICULAR APICAL PACING AND ITS FREQUENCY ON LEFT ATRIAL FUNCTION

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BACKGROUND: Right ventricular apical (RVA) pacing induces left ventricular (LV) dyssynchrony, increases the risk of persistent atrial fibrillation in the long term. The aim was to investigate the effects of RVA pacing on left atrial (LA) function, which are unknown.

METHODS: Echocardiographic evaluation including LV dyssynchrony based on conventional Doppler, tissue Doppler imaging and speckle tracking strain echocardiography was done before and after (12 months) single-chamber ventricular pacemaker implantation in 40 patients with sick sinus syndrome. Patients were divided to 2 groups, according to the RVA pacing frequency (group I had higher pacing rate of more than 50% and group II, less than 50%).

RESULTS: There was no significant difference in LV ejection fraction, however, mean global LV strain, myocardial performance index, and parameters of LV dyssynchrony had shown significant changes after 12 months of RVA pacing. There were also significant increase in the LA volume index and the reduction of peak systolic LA strain and strain rate (SR), peak early and late diastolic SR after RVA pacing. Moreover, there was significant deterioration of LV dyssynchrony and both LA and LV longitudinal function in even group II. LA functional deterioration and LA volume was significantly correlated with the frequency of RVA pacing.

CONCLUSION: LV dyssynchrony, induced by RVA pacing, significantly impaired active LA contraction and passive stretching, and these findings were shown in the patients with even less than 50% of RVA pacing. Impairment of LA strain/SR was significantly correlated with the frequency of RVA pacing.

KEY WORDS: Atrial function · Pacemaker · Dyssynchrony.

INTRODUCTION

Right ventricular apical (RVA) pacing, independently of pacing mode, can create an artificial inter-ventricular conduction delay and impairs left ventricular (LV) function.[1] Several large, randomized clinical trials on pacing mode selection have suggested an association between a high percentage of RVA pacing and increased risks of atrial fibrillation (AF) and heart failure in patients with sick sinus syndrome (SSS).[2-4] Long-term RVA pacing may also result in changes in LV wall thickness[5] and LV remodeling such as degenerative fibrosis.[6)7] In addition, functional mitral regurgitation and left atrial (LA) remodeling may occur during RVA pacing.[8)9]

However, it remains unclear whether the deterioration of LA function, as noted in a proportion of patients receiving RVA pacing, is directly related to LV dyssynchrony. Since assessment of myocardial longitudinal function based on strain echocardiography may be a sensitive marker for detecting subclinical alterations in LV and LA systolic performance,[10-12] we assessed the impact of chronic RVA pacing on LA function using tissue Doppler based strain echocardiography and association of LA strain parameters with LV mechanical dyssynchrony in the present study. We also aimed to know that patients can have significant myocardial functional benefit from lower frequency of RVA pacing compared with higher frequency of pacing.

METHODS

STUDY DESIGN AND SUBJECTS

We prospectively observed 40 patients who needed permanent pacemaker implantation for SSS between March 2008

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and October 2010. The study population consisted of single-chamber ventricular pacemaker (VVI mode) because of technical difficulties for the other types of pacemaker including dual chamber, and right ventricular outflow track pacing pacemakers. No patients had a history of ischemic heart disease, AF, bundle branch block, moderate to severe valvular heart disease, and systolic heart failure (LV ejection fraction < 50%).

Pacemaker follow-up was done at 1, 3, 6, and 12 months after implantation. The participants were divided into 2 groups according to the mean RVA pacing frequency (group I had higher pacing rate of more than 50% and group II, less than 50%), and echocardiographic variables as below were analyzed, as well. The study protocol was approved by the Institutional Review Committee on Human Research at Maryknoll Medical Center, and informed consent was obtained from all study subjects before participation.

Echocardiographic evaluation

A standard 2-dimensional and strain echocardiographic examination using a 2.5-MHz transducer on the Vivid 7 Dimension ultrasound equipment (General Electric, Horten, Norway) was performed on all subjects before and after (12 months) pacemaker implantation during normal sinus rhythm not ventricular pacing as possible.

Standard and Doppler echocardiography

Measurement of LV volume, LA volume and ejection fraction was calculated by the Simpson's methods from the apical 4- and 2-chamber views. Pulsed wave (PW) Doppler of transmitral LV inflow was performed in the apical 4-chamber view, with the sample volume placed at the level of the mitral valve tips and Doppler variables were analyzed during 3 consecutive beats. The following parameters of global LV diastolic function were determined: peak early (E) and late (A) diastolic mitral flow velocity and their ratio (E/A), early (Ea) diastolic mitral annular velocity, deceleration time of the E wave, and LV isovolumic relaxation time (IVRT). Doppler time intervals were measured from mitral inflow and LV outflow velocity-time intervals as described by Tei et al.[13] and the index of combined LV systolic and diastolic function (myocardial performance index) was calculated from the sum of isovolumic contraction time and IVRT divided by ejection time.

Strain echocardiography

Speckle tracking strain imaging (frame rate ≥ 70/sec) and tissue Doppler strain imaging (TDI, frame rate ≥ 115/sec) was performed in the apical 2-chamber, 3-chamber, and 4-chamber views using a narrow sector angle. Images from apical chamber views of the LV were obtained at end-expiratory apnea and were stored in cine-loop format for subsequent offline analysis. Three heartbeats were collected from each view and a selected 1-cycle was analyzed off-line with an EchoPAC Dimension system (General Electric, Horten, Norway).

Peak longitudinal systolic strains were measured and averaged to assess global longitudinal myocardial regional function. The endocardial borders were traced at the end-systolic frame, and an automated tracking algorithm outlined the myocardium in successive frames throughout the cardiac cycle. The tracking quality was verified for each segment (with subsequent manual adjustment of the region of interest, if necessary), and myocardial motion was analyzed by speckle tracking within the region of interest bound by endocardial and epicardial borders. Inadequate tracked segments were automatically excluded from analysis. In this situation, local strain in each segment was calculated. Global LV strain was obtained by averaging all segment strain values from the apical 4-chamber, 2-chamber, and long axis views.

For the LA strain, longitudinal peak strain and strain rate were obtained from 2 different areas of the basal segments of the LA free wall and the inter-atrial septum in the apical 4 chamber view by the tissue Doppler strain. For the longitudinal measurements, a computation area of 9 × 2 mm with an elliptical shape was chosen,[12] and mean peak systolic LA strain and strain rate (Sm-SR), peak early diastolic strain rate (Em-SR) and late diastolic strain rate (Am-SR) are measured.

Measurements of dyssynchrony

The inter-ventricular mechanical delay, calculated as difference between left pre-ejection interval (LPEI) and right pre-ejection interval (RPEI). LPEI is measured by PW Doppler in apical long axis projection and RPEI in short axis parasternal projection with sample volume in level of aortic (LPEI) or pulmonary (RPEI) valve. LPEI and RPEI is the interval from QRS beginning to start of ejection flow.[14]

For the intra-ventricular dyssynchrony, myocardial velocity curves are analyzed by tissue synchronization imaging in the apical 2-chamber, 3-chamber, and 4-chamber views. Using the 6-basal, 6-midsegmental LV model, the time from the onset of the QRS complex to peak systolic velocity in ejection period (Ts) are measured in each segment with 12 × 6 mm sample volume. The septal-to-lateral delay (Ts-SL), a TDI index proposed by Bax et al.,[15] is measured as the difference of Ts between the basal septal and lateral walls. The septal-to-posterior delay (Tε-SP) is measured as the time difference from the onset of the QRS complex and peak systolic radial strain wave between the anteroseptum and posterior walls at the parasternal short axis view by speckle tracking strain imaging.[16] Parameters of intra-ventricular dyssynchrony are calculated from Ts-SL or from the standard deviation of Ts (Ts-SD) among the 12 LV segments or Tε-SP.

Statistical analysis

Statistical analysis was performed with SPSS 15.0 package program (IBM Corp., Armonk, NY, USA). Results are presented as mean ± standard deviation. Paired Student's t-test was used for comparisons of continuous variables between before and after RVA pacing. Comparisons of all measurements were made with independent t-test for the parameters between group I and II. Correlations between variables were assessed by Pearson correlation, and p value of less than 0.05 was considered statistically significant.

Table 1. Clinical characteristics of study population

	SSS (n = 40)
Age (yr)	65.3 ± 10.2
Male, n (%)	15 (37.5%)
BMI (kg/m^2)	24.6 ± 2.6
SBP (mmHg)	123.1 ± 16.3
DBP (mmHg)	71.3 ± 12.3
Heart rate (/min)	69.4 ± 18.6
Hypertension, n (%)	23 (57.5%)
Diabetes mellitus, n (%)	7 (17.5%)
Smoking, n (%)	9 (22.5%)
Beta blocker, n (%)	6 (15.0%)
CCB, n (%)	21 (52.5%)
Statin, n (%)	20 (50.0%)
ACEi or ARB, n (%)	23 (57.5%)
Mean pacing frequency (%)	56.2 ± 42.8 (range 7.8-99.2%)

All values are presented as the mean ± SD. SSS: sick sinus syndrome, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, CCB: calcium channel blocker, ACEi: angiotensin-converting enzyme inhibitor, ARB: angiotensin II receptor blocker

RESULTS

CLINICAL CHARACTERISTICS OF SUBJECTS

Table 1 lists baseline characteristics of the 40 patients with SSS. The study population included 15 men and 25 women, with a mean age of 65.3 ± 10.2 years (range, 58-86 years). Twenty three patients had hypertension, 7 had diabetes mellitus, and 20 had dyslipidemia. Twenty one patients were on calcium-channel blockers, and 23 on angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. The range of ventricular pacing frequency was 7.8-99.2%.

LONG-TERM EFFECTS OF RVA PACING ON ECHOCARDIOGRAPHIC PARAMETERS

Table 2 showed the echocardiographic variables before and after 12 months of single-chamber ventricular RVA pacing. Although there was no significant change in LV volume and ejection fraction, the LV mass index, E/Ea, and LA volume index were significantly increased after RVA pacing. Also, there were significantly increased myocardial performance index

Table 2. Parameters of 2-dimensional and strain echocardiography before and after 12 months of RVA pacing

	Baseline (n = 40)	After 12 months (n = 40)	p
QRS duration (msec)	83.8 ± 14.7	90.4 ± 19.6	0.548
LV end systolic volume (mL)	42.3 ± 11.9	41.9 ± 12.6	0.866
LV end diastolic volume (mL)	98.6 ± 21.8	97.7 ± 22.3	0.907
LV mass index (gm/m^2)	120.08 ± 20.2	134.46 ± 31.9	0.043
Relative wall thickness	0.44 ± 0.05	0.46 ± 0.06	0.236
Ejection fraction (%)	66.2 ± 7.8	60.7 ± 6.04	0.089
Global LV strain (%)	-19.2 ± 6.23	-13.2 ± 4.65	0.012
Tei index	0.38 ± 0.08	0.45 ± 0.10	0.034
Inter-ventricular delay (msec)	25.7 ± 21.6	38.9 ± 22.7	0.041
Ts-SL (msec)	32.3 ± 12.8	60.9 ± 40.5	< 0.001
Ts-SD (msec)	29.8 ± 13.5	45.5 ± 18.3	0.002
Tε-SP (msec)	28.6 ± 26.7	48.9 ± 24.5	< 0.001
LA volume index (mL/m^2)	28.2 ± 8.4	38.8 ± 17.5	0.007
E velocity (cm/sec)	63.7 ± 24.0	75.7 ± 23.3	0.124
A velocity (cm/sec)	67.5 ± 10.3	73.5 ± 15.5	0.321
Ea velocity (cm/sec)	4.43 ± 1.13	5.88 ± 1.26	0.037
E/Ea	9.92 ± 4.9	14.1 ± 5.3	0.043
Peak systolic LA strain (%)	57.1 ± 9.8	35.3 ± 10.9	< 0.001
Sm-SR (sec^{-1})	3.01 ± 0.38	1.99 ± 0.52	< 0.001
Em-SR (sec^{-1})	-2.34 ± 0.18	-1.45 ± 0.37	< 0.001
Am-SR (sec^{-1})	-3.28 ± 0.42	-1.03 ± 0.29	< 0.001

Values are means ± SDs. RVA: right ventricular apical, LV: left ventricular, Ts: the time from the onset of the QRS complex to peak systolic velocity in ejection period, Ts-SL: the difference of Ts between the basal septal and lateral walls, Ts-SD: the standard deviation of Ts among the 12 LV segments, Tε-SP: the time difference from the onset of the QRS complex and peak systolic radial strain wave between the anteroseptum and posterior walls, LA: left atrial, E: peak early diastolic mitral flow velocity, A: peak early diastolic mitral flow velocity, Ea: peak early diastolic mitral annular velocity, Sm-SR: mean peak systolic strain rate, Em-SR: peak early diastolic strain rate, Am-SR: peak late diastolic strain rate and reduced global LV strain after RVA pacing as well as increased intra-ventricular delays of both TDI velocity and strain analysis (Table 2). The values of the peak systolic LA strain and Sm-SR, Em-SR and Am-SR were also significantly reduced after 12 months of RVA pacing.

Comparison of long-term effects of cumulative ventricular pacing percent on echocardiographic parameters

Table 3 showed the changes of the echocardiographic parameters before and after pacing in both groups. Average pacing frequency was undoubtedly different (group I: 89.4 ± 12.5 vs. group II: 25.9 ± 20.7%, $p < 0.001$). After pacing, the values of LV mass index and LA volume index were significantly higher in the group I, which was not demonstrated in the group II. However, there were significant differences in the value of global LV strain, myocardial performance index and intra-ventricular delays of both TDI velocity and strain analysis before and after RVA pacing in both group I and even in the group II (smaller pacing frequency group) (Table 3). Also, there were significantly increased E/Ea and reduced peak systolic LA srain, Sm-SR, Em-SR and Am-SR before and after RVA pacing in both group I and the group II (Table 3). Interestingly, there was significant difference in the intra-ventricular delays of both TDI velocity and strain analysis in favor of group II (Ts-SD; group II 40.2 ± 16.9 ms vs. group I 51.7 ± 14.7 ms, $p = 0.025$, Tε-SP; group II 46.6 ± 26.7 ms vs. group I 52.9 ± 24.5 ms, $p = 0.003$). Moreover, group I showed significantly lower global LV strain (-12.5 ± 4.92 vs. -15.9 ± 5.97%, $p = 0.023$) and peak LA systolic strain (28.2 ± 11.6 vs. 37.1 ± 10.4%, $p = 0.012$) compared with group II.

Correlation between the frequency of RVA pacing and the echocardiographic variables of LA function

There were significant correlations between the frequency of RVA pacing and the representative parameters of LA function, except for Ts-SD, and Em-SR (Table 4). Interestingly, the peak LA strain showed significant negative correlation with the pacing percentage (r = -0.425, p=0.028) (Table 4).

Discussion

Our study demonstrated that RVA pacing produce LV dyssynchrony and deterioration of LA and LV longitudinal function, as well. Moreover, there was significant reduction of LA and LV function even with lower frequency of RVA pacing, which might be more deteriorated with increased LV dyssynchrony induced by high frequency of RVA pacing.

Table 3. Two-dimensional and strain echocardiography parameters before and after 12 months RVA pacing according to the pacing percentage

	Group I (n = 22)			Group II (n = 18)		
	Baseline	After 12 months	*p*	Baseline	After 12 months	*p*
LV end systolic volume (mL)	42.1 ± 11.3	40.5 ± 12.4	0.354	42.8 ± 11.5	43.9 ± 12.5	0.486
LV end diastolic volume (mL)	97.8 ± 21.5	94.3 ± 13.9	0.573	98.9 ± 22.8	100.3 ± 12.1	0.762
LV mass index (gm/m^2)	120.37 ± 21.3	135.32 ± 28.7	0.034	119.54 ± 18.2	132.34 ± 33.9	0.062
Relative wall thickness	0.44 ± 0.05	0.46 ± 0.06	0.215	0.44 ± 0.04	0.46 ± 0.02	0.326
Ejection fraction (%)	66.9 ± 4.4	62.7 ± 6.04	0.089	65.8 ± 9.5	61.9 ± 4.01	0.476
Global LV strain (%)	-19.3 ± 3.3	-12.5 ± 4.92	0.023	-18.8 ± 9.6	-15.9 ± 5.97	0.043
Tei index	0.33 ± 0.11	0.46 ± 0.12	0.035	0.35 ± 0.18	0.42 ± 0.08	0.044
Inter-ventricular delay (msec)	25.6 ± 20.5	39.6 ± 21.9	0.006	25.3 ± 21.7	38.1 ± 23.1	0.037
Ts-SL (msec)	32.1 ± 13.2	63.2 ± 40.3	< 0.001	32.7 ± 11.9	57.6 ± 39.2	0.003
Ts-SD (msec)	33.4 ± 9.6	51.7 ± 14.7	< 0.001	32.3 ± 10.5	40.2 ± 16.9	0.032
Tε-SP (msec)	28.2 ± 8.9	52.9 ± 24.5	< 0.001	28.9 ± 9.7	46.6 ± 26.7	0.017
LA volume index	28.6 ± 9.5	43.9 ± 18.9	0.019	27.9 ± 8.3	32.1 ± 11.4	0.078
E velocity (cm/sec)	70.4 ± 25.7	75.8 ± 27.6	0.124	70.0 ± 21.8	63.7 ± 24.0	0.336
A velocity (cm/sec)	72.0 ± 16.0	75.6 ± 19.4	0.321	54.2 ± 21.6	68.3 ± 11.6	0.392
Ea velocity(cm/sec)	4.38 ± 1.21	6.02 ± 1.35	0.031	4.45 ± 1.32	5.99 ± 1.28	0.042
E/Ea	10.4 ± 3.52	15.8 ± 5.42	0.023	9.73 ± 3.68	12.2 ± 5.51	0.047
Peak systolic LA strain (%)	57.1 ± 9.54	28.2 ± 11.6	0.038	56.1 ± 7.36	37.1 ± 10.4	0.042
Sm-SR (sec^{-1})	3.03 ± 0.59	1.76 ± 0.51	< 0.001	3.12 ± 0.89	2.22 ± 0.55	0.048
Em-SR (sec^{-1})	-2.62 ± 0.52	-1.24 ± 0.45	< 0.001	-2.44 ± 0.17	-1.55 ± 0.27	0.043
Am-SR (sec^{-1})	-3.73 ± 0.62	-1.01 ± 0.28	0.023	-3.58 ± 0.49	-1.11 ± 0.23	0.034

Values are means ± SDs. RVA: right ventricular apical, LV: left ventricular, Ts: the time from the onset of the QRS complex to peak systolic velocity in ejection period, Ts-SL: the difference of Ts between the basal septal and lateral walls, Ts-SD: the standard deviation of Ts among the 12 LV segments, Tε-SP: the time difference from the onset of the QRS complex and peak systolic radial strain wave between the anteroseptum and posterior walls, LA: left atrial, E: peak early diastolic mitral flow velocity, A: peak early diastolic mitral flow velocity, Ea: peak early diastolic mitral annular velocity, Sm-SR: mean peak systolic strain rate, Em-SR: peak early diastolic strain rate, Am-SR: peak late diastolic strain rate

Table 4. Correlation between the frequency of RVA pacing and the echocardiographic variables of LA function

	r	95% CI	*p*
Ts-SL (msec)	0.234	0.106 - 0.362	0.039
Ts-SD (msec)	0.129	-0.007 - 0.248	0.052
Tε-SP (msec)	0.213	0.084 - 0.341	0.036
LA volume index (mL/m^2)	0.294	0.098 - 0.369	0.017
E/Ea	0.186	0.046 - 0.341	0.041
Peak systolic LA strain (%)	-0.425	-0.641 - -0.179	0.028
Sm-SR (sec^{-1})	-0.274	-0.495 - -0.132	0.037
Em-SR (sec^{-1})	0.117	-0.011 - 0.284	0.064
Am-SR (sec^{-1})	0.221	0.076 - 0.458	0.032

RVA: right ventricular apical, LA: left atrial, CI: confidence interval, Ts: the time from the onset of the QRS complex to peak systolic velocity in ejection period, Ts-SL: the difference of Ts between the basal septal and lateral walls, Ts-SD: the standard deviation of Ts among the 12 LV segments, Tε-SP: the time difference from the onset of the QRS complex and peak systolic radial strain wave between the anteroseptum and posterior walls, E: peak early diastolic mitral flow velocity, Ea: peak early diastolic mitral annular velocity, Sm-SR: mean peak systolic strain rate, Em-SR: peak early diastolic strain rate, Am-SR: peak late diastolic strain rate

LV functional change by RVA pacing and mechanical dyssynchrony

Animal studies have revealed dramatic mechanical effects from asynchronous electrical activation because the various regions differ not only in the time of onset of contraction but also in the pattern of contraction.[17] Early contracting regions close to the pacing site stretch remote regions that are not yet activated. This stretching further delays shortening of the late-activation regions. In clinical practice, RVA pacing therapy for bradycardia causes increase in heart failure and AF incidence through LV dyssynchrony.[18-21] Mechanical dyssynchrony is impacted by the myocardial architecture, not only electrophysiological but also histological and molecular factors. Therefore, it is speculated that the presence of different degrees of myocardial injury and interstitial fibrosis in different myocardial layers and segments of the failing heart would result in heterogeneous conduction abnormalities, which may increase its likelihood of developing mechanical dyssynchrony.

Echocardiographic strain imaging has been shown to be a useful tool to assess regional LV function, and useful to evaluate the effects of mechanical dyssynchrony on LV function because it can differentiate active thickening from passive wall motion. Our result shows the reduced global LV strain after 12 months RVA pacing indicating deterioration of LV systolic deformation as a result of asynchronous electrical activation by RVA pacing. Moreover, unexpectedly, reduced global LV strain was found even in the lower frequency of RVA pacing after 12 months, as well.

LA functional change by RVA pacing and mechanical dyssynchrony

Atrial function during early diastole is strongly influenced by the LV compliance,[22] and atrial function as reservoirs during systolic period is influenced by atrial relaxation. Booster pump function during late diastole is the intrinsic atrial contraction. LA dysfunction will be present even in a stage with slightly elevated LA pressure, and parameters of LA contractility assessed by conventional Doppler echocardiography are augmented in this stage; thus it will be difficult to detect LA dysfunction by this method. Our study shows similar mitral inflow filling patterns with non-significant increase in augmentation of late diastolic A velocity with RVA pacing.

The atrial walls consist of intricately intermingled muscular bundles oriented circumferentially and longitudinally[23] with individual contractility. TDI, as it measures myocardial velocities, displacement and deformation, has been shown to be less load-dependent regional quantitative parameters that reflect regional contraction and relaxation.[24] To date, not much data is available on atrial myocardial velocities, and our previous studies showed the role of values of LA strain/SR in diagnosis and management in patients with AF.[12)25] We chose to measure the TDI-based LA strain from the basal segments of the inter-atrial septum and the LA lateral wall, because it moves in a direction more parallel to the ultrasound beam and it is less affected by LV motion and translation. Analysis of the TDI-based LA strain demonstrated no significant difference in the septal wall and lateral wall. In this study, we found that there was significant increase in the LA volume index with increased E/Ea after RVA pacing, which implicating increased LV filling pressure. Moreover, the values of the peak systolic LA strain and Sm-SR, Em-SR and Am-SR were significantly reduced with RVA pacing. The possible mechanism is that the RVA pacing may increase inter-ventricular dyscoordination and LV depolarization times and consequently, the transmitral inflow during early diastole is compromised, which causes a larger residual volume before LA contraction. The presence of such volumetric changes and increased LA pressure might reduce longitudinal deformation, so the atrial lengthening that occurs during ventricular ejection is significantly reduced, and the atrial shortening that occurs during ventricular early filling is also reduced. Other studies have shown that LA pressure and volume overload resulted in significant up-regulation of beta-myosin heavy chain in the LA body associated with decreased velocity of LA contraction.[26)]

In our study, the peak systolic LA strain, Sm-SR, Em-SR and Am-SR were reduced by RVA pacing, which implies an impaired passive lengthening (stretching) and shortening of the atrial walls, and this is possibly because of increased residual volume with reduced compliance and increased pressure. Moreover, the reduced LA strain parameters were found even in the lower frequency of RVA pacing after 12 months, as well. However, the significant negative correlation between the frequency of RVA pacing and the peak systolic LA strain/SR implicate the deterioration of LA function might be exacerbated by high ventricular pacing.

Study limitations

Although we tried to assess LA function by strain echocardiography, LA function also could be evaluated by the phasic volume, so the simultaneous measurement of LA phasic volume and LA strain variables might provide the more accurate LA functional change induced by mechanical dyssynchrony. Secondary, separate measurement of intraventricular and interventricular synchrony index and strain parameters during with narrow QRS and wide QRS would be helpful to know the effect of RVA pacing-induced dyssynchrony or RVA pacing itself on LA. Finally, although we sought to evaluate the pure effect of RVA pacing on myocardial performance, the number of patients was so small. Large scale multicenter trial is definitely necessary to test our results.

Conclusion

After 12 months of single-chamber ventricular pacemaker implantation, significant deterioration of global LV function with LV mechanical dyssynchrony was induced, which may play a role in the development of heart failure. Moreover, LA volume and pressure burden brought by RVA pacing caused an impairment of LA active contraction and passive stretching, assessed by strain echocardiographic parameters, even in the lower pacing percentage group. There were significant correlations between the cumulative percentage of RVA pacing and the representative parameters of LA active contraction and passive stretching, as well.

References

1. Schmidt M, Brömsen J, Herholz C, Adler K, Neff F, Kopf C, Block M. *Evidence of left ventricular dyssynchrony resulting from right ventricular pacing in patients with severely depressed left ventricular ejection fraction. Europace 2007;9:34-40.*
2. Sweeney MO, Hellkamp AS, Ellenbogen KA, Greenspon AJ, Freedman RA, Lee KL, Lamas GA; MOde Selection Trial Investigators. *Adverse effect of ventricular pacing on heart failure and atrial fibrillation among patients with normal baseline QRS duration in a clinical trial of pacemaker therapy for sinus node dysfunction. Circulation 2003;107:2932-7.*
3. Wilkoff BL, Cook JR, Epstein AE, Greene HL, Hallstrom AP, Hsia H, Kutalek SP, Sharma A; Dual Chamber and VVI Implantable Defibrillator Trial Investigators. *Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: the Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA 2002;288:3115-23.*
4. Steinberg JS, Fischer A, Wang P, Schuger C, Daubert J, McNitt S, Andrews M, Brown M, Hall WJ, Zareba W, Moss AJ; MADIT II Investigators. *The clinical implications of cumulative right ventricular pacing in the multicenter automatic defibrillator trial II. J Cardiovasc Electrophysiol 2005;16:359-65.*
5. van Oosterhout MF, Prinzen FW, Arts T, Schreuder JJ, Vanagt WY, Cleutjens JP, Reneman RS. *Asynchronous electrical activation induces asymmetrical hypertrophy of the left ventricular wall. Circulation 1998;98:588-95.*
6. Karpawich PP, Rabah R, Haas JE. *Altered cardiac histology following apical right ventricular pacing in patients with congenital atrioventricular block. Pacing Clin Electrophysiol 1999;22:1372-7.*
7. Vernooy K, Dijkman B, Cheriex EC, Prinzen FW, Crijns HJ. *Ventricular remodeling during long-term right ventricular pacing following His bundle ablation. Am J Cardiol 2006;97:1223-7.*
8. Barold SS, Ovsyshcher IE. *Pacemaker-induced mitral regurgitation. Pacing Clin Electrophysiol 2005;28:357-60.*
9. Maurer G, Torres MA, Corday E, Haendchen RV, Meerbaum S. *Two-dimensional echocardiographic contrast assessment of pacing-induced mitral regurgitation: relation to altered regional left ventricular function. J Am Coll Cardiol 1984;3:986-91.*
10. Nishikage T, Nakai H, Lang RM, Takeuchi M. *Subclinical left ventricular longitudinal systolic dysfunction in hypertension with no evidence of heart failure. Circ J 2008;72:189-94.*
11. Cho GY, Song JK, Park WJ, Han SW, Choi SH, Doo YC, Oh DJ, Lee Y. *Mechanical dyssynchrony assessed by tissue Doppler imaging is a powerful predictor of mortality in congestive heart failure with normal QRS duration. J Am Coll Cardiol 2005;46:2237-43.*
12. Cho KI, Lee HG, Ak SJ, Huh JE, Kim HJ, Moon JY, Park KM, Kim TI. *Quantitative assessment of left atrial functional changes in patients with atrial fibrillation by tissue Doppler strain and 2-dimensional strain imaging. Korean Circ J 2006;36:786-93.*
13. Tei C, Ling LH, Hodge DO, Bailey KR, Oh JK, Rodeheffer RJ, Tajik AJ, Seward JB. *New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function--a study in normals and dilated cardiomyopathy. J Cardiol 1995;26:357-66.*
14. Cazeau S, Bordachar P, Jauvert G, Lazarus A, Alonso C, Vandrell MC, Mugica J, Ritter P. *Echocardiographic modeling of cardiac dyssynchrony before and during multisite stimulation: a prospective study. Pacing Clin Electrophysiol 2003;26:137-43.*
15. Bax JJ, Marwick TH, Molhoek SG, Bleeker GB, van Erven L, Boersma E, Steendijk P, van der Wall EE, Schalij MJ. *Left ventricular dyssynchrony predicts benefit of cardiac resynchronization therapy in patients with end-stage heart failure before pacemaker implantation. Am J Cardiol 2003;92:1238-40.*
16. Tops LF, Suffoletto MS, Bleeker GB, Boersma E, van der Wall EE, Gorcsan J 3rd, Schalij MJ, Bax JJ. *Speckle-tracking radial strain reveals left ventricular dyssynchrony in patients with permanent right ventricular pacing. J Am Coll Cardiol 2007;50:1180-8.*
17. Prinzen FW, Peschar M. *Relation between the pacing induced sequence of activation and left ventricular pump function in animals. Pacing Clin Electrophysiol 2002;25:484-98.*
18. Connolly SJ, Kerr CR, Gent M, Roberts RS, Yusuf S, Gillis AM, Sami MH, Talajic M, Tang AS, Klein GJ, Lau C, Newman DM. *Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. Canadian Trial of Physiologic Pacing Investigators. N Engl J Med 2000;342:1385-91.*

19. Cho GY, Kim MJ, Park JH, Kim HS, Youn HJ, Kim KH, Song JK. *Comparison of ventricular dyssynchrony according to the position of right ventricular pacing electrode: a multi-center prospective echocardiographic study. J Cardiovasc Ultrasound 2011;19:15-20.*
20. Toff WD, Camm AJ, Skehan JD; United Kingdom Pacing and Cardiovascular Events Trial Investigators. *Single-chamber versus dual-chamber pacing for high-grade atrioventricular block. N Engl J Med 2005;353:145-55.*
21. Healey JS, Toff WD, Lamas GA, Andersen HR, Thorpe KE, Ellenbogen KA, Lee KL, Skene AM, Schron EB, Skehan JD, Goldman L, Roberts RS, Camm AJ, Yusuf S, Connolly SJ. *Cardiovascular outcomes with atrial-based pacing compared with ventricular pacing: meta-analysis of randomized trials, using individual patient data. Circulation 2006; 114:11-7.*
22. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. *Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. Am J Cardiol 2002; 90:1284-9.*
23. Wang K, Ho SY, Gibson DG, Anderson RH. *Architecture of atrial musculature in humans. Br Heart J 1995;73:559-65.*
24. Hatle L, Sutherland GR. *Regional myocardial function--a new approach. Eur Heart J 2000;21:1337-57.*
25. Cho KI, Lee SH, Jang SH, Lee DW, Lee HG, Kim TI. *Assessment of left atrial function and remodeling in patients with atrial fibrillation by performing strain echocardiography: a prospective study to assess the influence of renin-angiotensin system inhibitors on atrial fibrillation. Korean Circ J 2008;38:305-12.*
26. Hoit BD, Shao Y, Gabel M, Walsh RA. *Left atrial mechanical and biochemical adaptation to pacing induced heart failure. Cardiovasc Res 1995;29:469-74.*