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Energy loss by right ventricular pacing: Patients with versus without hypertrophic cardiomyopathy

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Abstract

Background: Right ventricular (RV) pacing causes left ventricular (LV) dyssynchrony sometimes resulting in pacing-induced cardiomyopathy. However, RV pacing for hypertrophic obstructive cardiomyopathy is one of the treatment options. LV flow energy loss (EL) using vector flow mapping (VFM) is a novel hemodynamic index for assessing cardiac function. Our study aimed to elucidate the impact of RV pacing on EL in normal LV function and hypertrophic cardiomyopathy (HCM) patients.

Methods: A total of 36 patients with dual-chamber pacemakers for sick sinus syndrome or implantable cardioverter defibrillators for fatal ventricular tachyarrhythmias were enrolled. All patients were divided into two groups: 16 patients with HCM (HCM group) and others (non-HCM group). The absolute changes in EL under AAI (without RV pacing) and DDD (with RV pacing) modes were assessed using VFM on color Doppler echocardiography.

Results: In the non-HCM group, the mean systolic EL significantly increased from the AAI to DDD modes (14.0 ± 7.7 to 17.0 ± 8.6 mW/m, $P = .003$), whereas the mean diastolic EL did not change (19.0 ± 12.3 to 17.0 ± 14.8 mW/m, $P = .231$). In the HCM group, the mean systolic EL significantly decreased from the AAI to DDD modes (26.7 ± 14.2 to 21.6 ± 11.9 mW/m, $P < .001$), whereas the mean diastolic EL did not change (28.7 ± 16.4 to 23.9 ± 19.7 mW/m, $P = .130$).

Conclusions: RV pacing increased the mean systolic EL in patients without HCM. Conversely, RV pacing decreased the mean systolic EL in patients with HCM.

KEYWORDS

echocardiography, energy loss, hypertrophic cardiomyopathy, right ventricular pacing, vector flow mapping

1 | INTRODUCTION

Pacing therapy is beneficial for brady arrhythmias.[1,2] However, it has been reported that nonphysiologic right ventricular (RV) pacing could cause left ventricular (LV) systolic dysfunction, and pacing-induced cardiomyopathy (PICM).[3,4] Abnormal electrical and mechanical asynchronous activation has been suggested as a cause of PICM, but has not yet been fully explained.[5] However, RV pacing for hypertrophic obstructive cardiomyopathy (HOCM) is considered as one of the treatment options.[6] Dyssynchrony of the LV wall motion by RV pacing conceptually ameliorates LV outflow obstruction, but the detailed mechanisms of this effect also remain unclear. Vector flow mapping (VFM) is a novel echocardiographic method that enables to visualize the intraventricular blood flow using color Doppler and speckle tracking data, and has proved to be an accurate tool for depicting and measuring in vitro generated flow structures.[7,8] The flow dissipative energy loss (EL) is estimated by VFM. The EL is caused by viscous friction between the flowing blood and wall shear flow, which converts kinetic energy to heat. A greater EL is observed with more rapid changes in the blood flow velocity and direction.[9,10] Previous research demonstrated that the prevalence of diabetes mellitus,[11] chronic kidney disease,[12] valvular heart disease,[13,14] and ischemic heart disease[15] were correlated with increases in the EL. However, the impact of RV pacing on the EL has not been fully elucidated. In this study, we investigated the effect of RV apical (RVa) pacing on the EL in patients without structural abnormality and those with hypertrophic cardiomyopathy (HCM).

2 | METHODS

2.1 | Study population

A total of 70 patients who underwent dual-chamber pacemaker (PM) or implantable cardioverter defibrillator (ICD) implantation were investigated. Fifty-four consecutive patients without HCM and three patients with HCM who underwent echocardiography with VFM during hospitalization for a device implantation from May 2017 to April 2019 were enrolled, and to focus on the HCM patients, 13 consecutive ambulant patients with HCM in whom devices had been previously implanted were also enrolled in the study. These patients underwent echocardiography with VFM at an outpatient clinic. To reveal the effect of nonphysiological RVa pacing, patients with a preserved intrinsic atrioventricular (AV) conduction and left ventricular ejection fraction (LVEF) were assigned. Consequently, 34 patients were excluded for the following reasons: 1) four patients had a reduced LV systolic function (LVEF ≤ 50%), 2) 25 patients lacked a preserved intrinsic atrioventricular conduction as a result of advanced or complete AV block, 3) two patients were diagnosed with other cardiomyopathies, 4) one patient lacked data, and 5) two patients had poor echocardiographic images. A total of 36 patients were ultimately enrolled in this study (Figure 1). All of the ventricular pacing leads were placed at the RV apex. To unify the heart rate's effect,

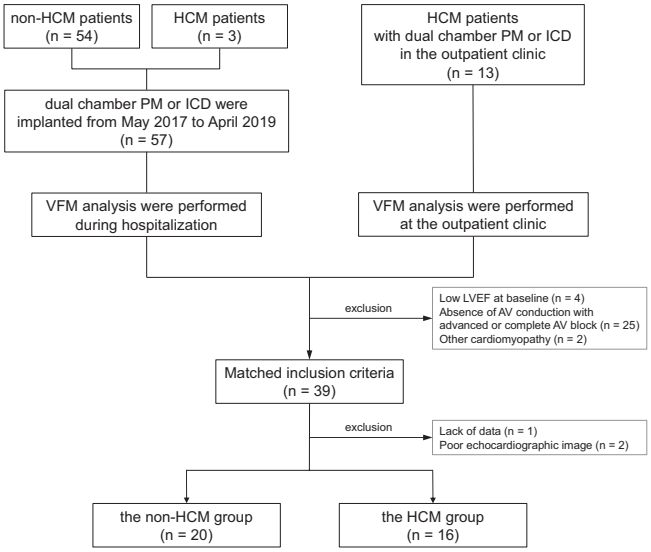

FIGURE 1 Study protocol. PM, pacemaker; ICD, implantable cardioverter defibrillator; HCM, hypertrophic cardiomyopathy; LVEF, left ventricular ejection fraction; AV block, atrioventricular block

the atrial pacing rate was programmed to 90 beats per minute in all of the patients during the echocardiographic evaluation. The HCM group was defined as patients with HCM. The HCM diagnosis was based on the reported definitions,[16,17] that is, segmental left ventricular hypertrophy (thickness ≥ 15 mm) measured by any imaging technique (echocardiography, computed tomography, or cardiac resonance imaging) without other causes of wall thickening. An LV outflow tract (LVOT) obstruction was defined as a peak instantaneous Doppler LVOT gradient ≥30 mmHg.[17] The patients without HCM were classified as the non-HCM group in this study. In the non-HCM group, 17 patients were implanted with dual-chamber PMs for sick sinus syndrome (SSS), and three were implanted with ICDs for ventricular fibrillation (VF). In the HCM group, three patients were implanted with dual-chamber PMs for SSS, one was implanted with a dual-chamber PM for intermittent AV block, and 12 were implanted with ICDs for ventricular tachycardia or VF. This study was reviewed and approved by the institutional review boards of Kitasato University Hospital.

2.2 | Echocardiographic evaluation

Echocardiographic examinations were conducted in the left lateral supine position using standard sequences on an ALOKA LISENDO 880 device (Hitachi Aloka Medical Ltd., Tokyo, Japan). The LV end-diastolic dimensions, LV end-systolic dimensions, and left atrial dimensions were measured in the M or B modes in the parasternal long- and short-axis views. The LVEF was measured by the modified Simpson's method on images in the apical 4-chamber views. Using pulsed-wave Doppler echocardiography, the early diastole (E wave) and atrial contraction (A wave) phases of the LV filling were evaluated. To evaluate the early diastolic velocity at the mitral annulus

(e') and E/e' ratio, the pulsed-wave tissue Doppler velocities were measured at the septal mitral annulus in the 4-chamber view. Color Doppler data for the VFM analysis were obtained in the apical 3-chamber view with and without RVa pacing. The image width and depth were adjusted to display the entire LV inflow tract, LV cavity, LV outflow, and mitral and aortic valves. The spatiotemporal settings were optimized to achieve the highest possible frame rate. A Doppler velocity range of −66 to 66 cm/s was selected for this study. Three consecutive heartbeats were stored digitally on a built-in hard disk, and analyzed using VFM analysis software (DAS-RS1, Hitachi Aloka Medical Ltd., Tokyo, Japan).[5]

2.3 | Flow visualization and EL analysis

To evaluate the effect of RVa pacing on the EL, a single-chamber atrial pacing (AAI) mode preset to 90 beats per minute for atrial pacing and a dual-chamber pacing (DDD) mode with the same preset atrial pacing rate were used. In the DDD mode, the AV delay was set to a range of 120 to 150 msec throughout the RV pacing. The LV intracardiac flow was recorded in the apical 3-chamber view by color Doppler imaging. The left ventricular endocardial border was manually traced to identify the velocity of the wall motion by speckle tracking. The pulse frequency of the color Doppler image was set to avoid aliasing. If aliasing was observed, the aliased area was manually corrected. The intraventricular flow velocity vectors were determined from the wall velocities and color Doppler velocity data. The velocity vector of the LV intracavitary blood flow was computed by the software based on a system developed by Itatani et al[18] Based on the VFM images, the intraventricular EL, vortex area, and circulation were calculated.[13,19] The definitions of the vortex area and circulation were based on previous reports,[20-22] that is, the vortex area was defined as the largest area of the physiological vortex measured during each cardiac cycle, and the circulation was calculated as the integral of the vorticity over an area. The circulation represented the quantity of flow swirling inside the vortex in the observed plane.[21] When the presence of a vortex was detected, the vortex area and the circulation were automatically calculated by the software. The intracardiac EL was calculated as the average of one cardiac cycle (ELcycle), and we also separately evaluated the systolic EL (ELsys) and diastolic EL (ELdia). All of the data were analyzed in both the AAI and DDD modes. Three consecutive cycles were captured in one recording. Each parameter was defined as the mean of three consecutive cardiac cycles. One cardiac cycle image was selected for analysis between two consecutive electrocardiogram QRS complexes. The cardiac phase was determined by the combination of the echocardiography valve openings. If the valve opening image quality was insufficient to assess, the timing of the ECG parameters was auxiliary utilized. The isovolumetric contraction (IVC) period was defined as the mitral valve closure to aortic valve opening, and the isovolumic relaxation period was defined as the aortic valve closure to mitral valve opening. Systole was distinguished from diastole by the first frame just after the closure of the aortic valve.

2.4 | Statistical analysis

Continuous variables are described as the mean ± standard deviation. Categorical variables are reported as counts with percentages (%). The Wilcoxon signed-rank test was used when comparing the data between the AAI and DDD modes, and the Pearson's chi-squared test or the Mann-Whitney U-test was used in the comparison between the non-HCM and HCM groups. In all of the analyses, p values of <0.05 were defined as statistically significant. All statistical analyses were performed with JMP software version 13.2 (SAS Institute, Cary, NC, USA).

3 | RESULTS

3.1 | Baseline characteristics

The two groups baseline characteristics are shown in Table 1. The HCM group included two cases of apical hypertrophy (apical hypertrophy alone), 11 cases of septal hypertrophy (septal hypertrophy alone or septal hypertrophy with hypertrophy of the adjacent segments), and three cases of diffuse hypertrophy. Four patients in the group were diagnosed with HOCM. In three of those patients, the LVOT pressure gradient was ameliorated by appropriate medical treatment, whereas one patient still had a significant LVOT pressure gradient. There were no significant differences in the baseline characteristics between the two groups except for the age at time of the device implantation (Table 1). The laboratory data and electrocardiographic and echocardiographic findings are shown in Table 2. The HCM group had significantly longer intraventricular septum dimensions (17.1 ± 3.8 vs 10.6 ± 1.6 mm, $P < .001$), longer posterior wall dimensions (12.6 ± 3.5 vs 10.2 ± 1.5 mm, $P = .031$), and larger E/e' (16.0 ± 7.3 vs 10.9 ± 3.6, $P = .020$) than the non-HCM group.

TABLE 1 Baseline patient characteristics of patients with non-HCM group and HCM group

	non-HCM (n = 20)	HCM (n = 16)	*P* value
Age at implantation, y	77.0 ± 7.8	66.4 ± 14.7	.043
Male, n (%)	8 (40)	9 (56)	.503
Height, cm	155.6 ± 7.5	160.7 ± 9.2	.074
Weight, kg	54.7 ± 10.9	58.4 ± 12.1	.381
Systolic BP, mmHg	119.7 ± 15.5	120.5 ± 17.9	.811
Diastolic BP, mmHg	69.6 ± 13.1	72.4 ± 13.8	.799
Hypertension, n (%)	14 (70)	6 (38)	.091
Hyperlipidemia, n (%)	12 (60)	7 (44)	.503
Diabetes mellitus, n (%)	9 (45)	2 (13)	.067
Ischemic heart disease, n (%)	6 (30)	2 (13)	.257
Chronic kidney disease, n (%)	4 (20)	7 (44)	.159
Smoking, n (%)	8 (40)	7 (44)	1.000

Note: Values are mean ± SD or n (%).

Abbreviations: BP, blood pressure; HCM, hypertrophic cardiomyopathy.

TABLE 2 Laboratory data, electrocardiography and echocardiography findings

	non-HCM (n = 20)	HCM (n = 16)	*P* value
Laboratory data			
HbA1c, %	6.11 ± 0.65	5.94 ± 0.80	.321
eGFR, mL/min/1.73m^2	53.9 ± 21.0	53.3 ± 18.5	.524
Cr, mg/dL	1.16 ± 0.98	1.05 ± 0.30	.108
BNP, pg/mL	202.8 ± 250.3	364.4 ± 239.8	.033
Electrocardiography			
QRS duration (AAI), msec	101.3 ± 18.0	121.6 ± 25.8	.015
QRS duration (DDD), msec	159.8 ± 23.5	178.0 ± 29.9	.301
Echocardiography			
LVDd (AAI), mm	44.6 ± 5.5	46.3 ± 7.4	.394
LVDs (AAI), mm	26.2 ± 4.7	26.5 ± 5.7	.907
LVDd (DDD), mm	43.6 ± 4.8	43.9 ± 7.6	.962
LVDs (DDD), mm	26.9 ± 3.8	26.6 ± 6.6	.632
LAD, mm	36.0 ± 6.4	40.0 ± 5.8	.062
IVS, mm	10.5 ± 1.6	17.1 ± 3.8	<.0001
PW, mm	10.2 ± 1.6	12.6 ± 3.5	.031
LVEF (AAI), %	67.0 ± 8.3	61.4 ± 9.1	.046
LVEF (DDD), %	62.1 ± 6.4	59.8 ± 6.8	.332
LVOT-VTI (AAI), cm	18.1 ± 5.8	19.3 ± 3.2	.616
LVOT-VTI (DDD), cm	18.3 ± 3.7	19.3 ± 3.8	.523
E, cm/sec	55.1 ± 21.6	70.0 ± 26.3	.083
A, cm/sec	73.6 ± 18.7	76.9 ± 46.1	.762
E/e'	10.9 ± 3.6	16.0 ± 7.3	.020

Note: Values are mean ± SD or n (%).

Abbreviations: BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; HCM, hypertrophic cardiomyopathy; IVS, intraventricular septum; LAD, left atrial dimension; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; LVOT-VTI, left ventricular outflow tract velocity time integral; PW, posterior wall.

Likewise, the QRS duration before the device implantation was longer in the HCM group than in the non-HCM group (121.6 ± 25.8 vs 101.3 ± 18.0 msec, $P = .015$). The QRS duration after the device implantation was comparable between the two groups (178.0 ± 29.9 vs 159.8 ± 23.5 msec, $P = .301$). There were no significant differences in the other parameters.

3.2 | Absolute change in the LV blood flow and EL by RVa pacing

Figure 2 shows representative images of the absolute changes in the LV blood flow (panel A) and EL (panel B) by a change from the AAI to DDD modes, that is, that with and without RVa pacing. In the non-HCM group (panel A-a and A-c), RVa pacing reduced the vortex area and circulation during the IVC period. Conversely, in the HCM group (panel A-b and A-d), RVa pacing enlarged the vortex area and strengthened the circulation during the IVC period, suggesting that RVa pacing improved the flow dynamics in the HCM group. RVa pacing increased the ELsys in the non-HCM group (10.7 mW/m in AAA to 15.8 mW/m in DDD, panel B-a), but decreased it in the HCM group (14.7 mW/m to 12.5 mW/m, panel B-b). The results of the EL analyses are shown in Table 3. During the AAI mode (without RVa pacing), the ELcycle and ELsys were significantly lower in the non-HCM group than in the HCM group, whereas the ELdia was comparable between the two groups. The percent change in the ELcycle and ELsys from the AAI to DDD modes was significantly higher in the non-HCM group than in the HCM group. The changes in the EL by RVa pacing in both groups are shown in Figure 3. In the non-HCM group (upper panels), the ELsys significantly increased from the AAI to DDD modes (14.0 ± 7.7 to 17.0 ± 8.6 mW/m, $P = .003$). In the HCM group (lower panels), the ELsys significantly decreased from the AAI to DDD modes (26.7 ± 14.2 to 21.6 ± 11.9 mW/m, $P = .009$). Although the HCM group included various types of HCM, the EL data changes from the AAI to DDD modes in each case showed similar trends. In both groups, the ELdia did not significantly change from the AAI to DDD modes. The LV vortex flow analyses in both groups are shown in Table 4. In the non-HCM group, the vortex area during the IVC period had a tendency to be smaller when changing from the AAI to DDD modes (452.7 ± 229.1 to 387.5 ± 201.8 mm^2, $P = .30$).

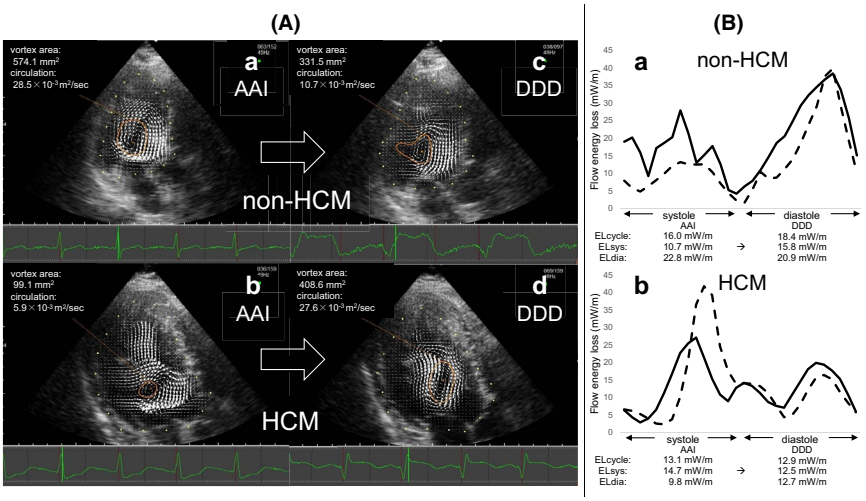

FIGURE 2 Representative images of the vortex during the IVC period and changes in the EL by RVa pacing in the non-HCM and HCM groups. Representative changes in the vortex during the IVC period (panel A) and EL (panel B) by RVa pacing in the non-HCM and HCM groups. The dotted lines show the ELcycle during the AAI mode, and the solid lines show that in the DDD mode (panel B). In the non-HCM group, RVa pacing reduced the vortex area and circulation during the IVC period (panels A-a and c), and increased the ELsys (panel B-a). Conversely, in the HCM group, RV pacing enlarged the vortex area and circulation during the IVC period (panels A-b and d), and decreased the ELsys (panel B-b). IVC, isovolumetric contraction; EL, energy loss; ELcycle, EL over one cardiac cycle; ELsys, systolic EL; ELdia, diastolic EL; RVa pacing, right ventricular apical pacing; HCM, hypertrophic cardiomyopathy; AAI, single-chamber pacing; DDD, dual-chamber pacing; RVa pacing, right ventricular apical pacing

TABLE 3 mean EL in the non-HCM group and the HCM group

	non-HCM (n = 20)	HCM (n = 16)	*P* value
ELcycle with AAI mode, mW/m	16.7 ± 9.2	28.4 ± 12.6	.007
ELcycle with DDD mode, mW/m	17.7 ± 10.9	23.2 ± 13.2	.214
ELsys with AAI mode, mW/m	14.0 ± 7.7	26.7 ± 14.2	.005
ELsys with DDD mode, mW/m	17.0 ± 8.6	21.6 ± 11.9	.445
ELdia with AAI mode, mW/m	19.0 ± 12.3	28.7 ± 16.4	.111
ELdia with DDD mode, mW/m	17.0 ± 14.8	23.9 ± 19.7	.192
%change of ELcycle by pacing, %	3.6 ± 20.3	-20.1 ± 18.3	.005
%change of ELsys by pacing, %	26.9 ± 32.8	-14.2 ± 26.1	<.001
%change of ELdia by pacing, %	-14.2 ± 33.9	-19.9 ± 39.9	.702

Note: Values are mean ± SD or n (%). %change denotes percentage change of EL from AAI to DDD mode.

Abbreviations: EL, energy loss; ELcycle, EL over one cardiac cycle; ELdia, diastolic EL; ELsys, systolic EL; HCM, hypertrophic cardiomyopathy.

Conversely, in the HCM group, the vortex area during the IVC period was significantly larger when changing from the AAI to DDD modes (270.4 ± 161.0 to 450.7 ± 151.4 mm^2, $P = .016$). The percent changes in the vortex area and circulation caused by the RVa pacing are shown in Figure 4. They significantly increased by RVa pacing in the HCM group as compared to that in the non-HCM group (116.7 ± 164.3 vs −15.3 ± 29.2%, $P < .001$; 133.4 ± 192.9 vs −11.5 ± 40.8%, $P < .001$).

4 | DISCUSSION

The main findings of this study were as follows: during RVa pacing, 1) the ELsys significantly increased in the non-HCM group, and 2) the ELcycle and ELsys significantly decreased in the HCM group. In the detailed evaluation, the vortex area and circulation detected by VFM decreased in the non-HCM group, but increased in the HCM group.

4.1 | Changes in the EL by RVa pacing

In the VFM analysis in the non-HCM group, energetically efficient vortices formed in the left ventricle. Those vortices facilitate the inflow into the ventricle, minimize the dissipation of energy, preserve the momentum, and redirect the flow toward the LV outflow.[9,23] In diastole, clockwise and counterclockwise vortices form around the mitral valve. Counterclockwise vortices quickly disappear, and

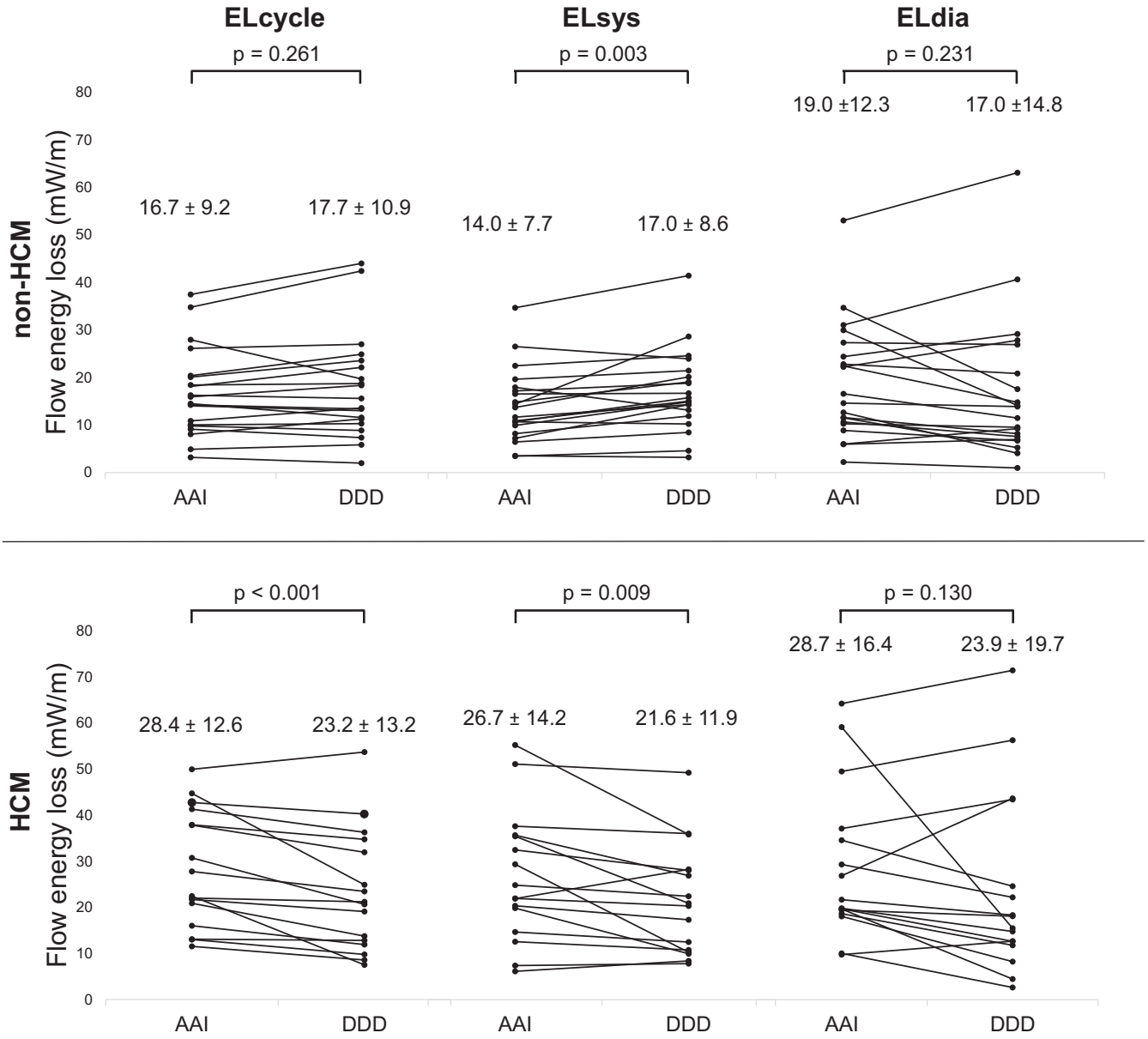

FIGURE 3 Changes in the EL by RVa pacing in the non-HCM and HCM groups. In the non-HCM group, the ELsys significantly increased from the AAI to DDD modes. The ELcycle and ELdia did not change from the AAI to DDD modes (upper panels). In the HCM group, the ELcycle and ELsys significantly decreased from the AAI to DDD modes. The ELdia did not change from the AAI to DDD modes (lower panels). EL, energy loss; ELcycle, EL over one cardiac cycle; ELsys, systolic EL; ELdia, diastolic EL; RVa pacing, right ventricular apical pacing; HCM, hypertrophic cardiomyopathy; AAI, single-chamber atrial pacing; DDD, dual-chamber pacing

clockwise vortices remain until the IVC period. In systole, a large vortex at the base portion during the IVC period promotes an efficient ejection. An intraventricular EL is caused by viscous friction produced by the disturbance of the vector and velocity of the blood flow. Li et al reported that the intraventricular EL was a sensitive indicator of preclinical LV dysfunction in patients with an early stage of diabetic cardiomyopathy with diastolic dysfunction.[11] Previous studies demonstrated that the physiological vortex patterns changed, followed by an increase in the EL in patients with valvular heart disease[13,14] and ischemic heart disease.[15] Thus, it is assumed that evaluations of the changes in the vortices and EL using VFM are useful for predicting LV dysfunction. However, the impact of RVa pacing on the physiological vortices and EL remains unclear. In this study, we focused on RVa pacing in HCM and non-HCM patients and demonstrated that RVa pacing significantly increased the ELsys in the non-HCM group and conversely decreased the ELcycle and ELsys in the HCM group.

4.2 | Mechanisms of the EL increase by RVa pacing in the non-HCM group

The cause of adverse effects by nonphysiologic RVa pacing on the LV systolic function has not been fully elucidated. Several studies of the effects of RVa pacing have been reported. Ventricular

TABLE 4 LV vortex flow analysis in the non-HCM group and the HCM group

	AAI	DDD	*P* value
In non-HCM group			
VORTEX area in IVC period, mm^2	452.7 ± 229.1	387.5 ± 201.8	.300
Circulation, in IVC period, m^2/sec	$14.0 \times 10^{-3} \pm 9.5 \times 10^{-3}$	$12.9 \times 10^{-3} \pm 9.4 \times 10^{-3}$	.651
In HCM group			
Vortex area in IVC period, mm^2	270.4 ± 161.0	450.7 ± 151.4	.016
Circulation, in IVC period, m^2/sec	$11.2 \times 10^{-3} \pm 6.9 \times 10^{-3}$	$19.5 \times 10^{-3} \pm 7.2 \times 10^{-3}$	.006

Note: Values are mean ± SD.

Abbreviations: AAI, single-chamber atrial pacing; DDD, dual-chamber pacing; HCM, hypertrophic cardiomyopathy; IVC, isovolumetric contraction.

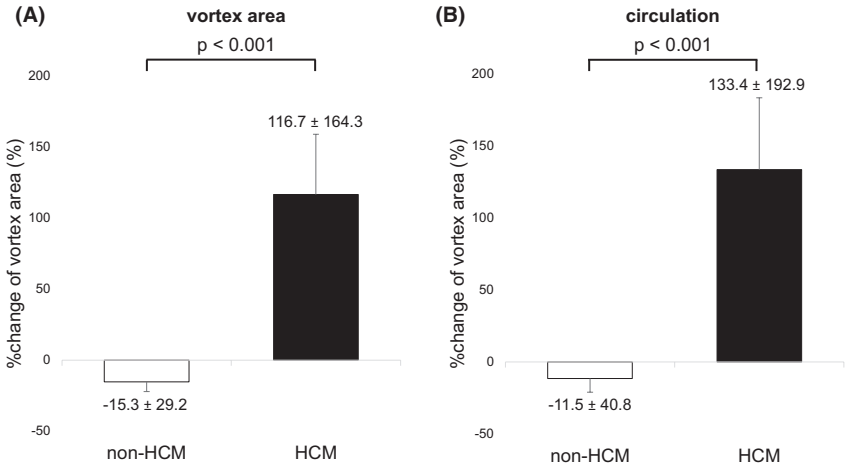

FIGURE 4 Percent change in the vortex area and circulation by RVa pacing in the IVC period between the non-HCM and HCM groups. The percent changes in the vortex area (panel A) and circulation (panel B) by RVa pacing between the non-HCM and HCM groups. Compared with the non-HCM group, the HCM group had a significantly increased percent change in the vortex area and circulation during the IVC period. RVa pacing, right ventricular apical pacing; IVC, isovolumetric contraction; HCM, hypertrophic cardiomyopathy

dyssynchrony by RVa pacing results in asymmetric hypertrophy and a redistribution of the cardiac mass,[24] mitral regurgitation,[25,26] increased left atrial diameter,[27] and reduced ejection fraction.[28-30] Changes in the cardiac metabolism, coronary perfusion, LV remodeling, and impaired hemodynamics by RVa pacing have also been reported.[1] In this study, RVa pacing significantly prolonged the QRS duration in the non-HCM group (101.3 ± 18.0 to 159.8 ± 23.5 msec, $P < .0001$). In this study, nonphysiological ventricular conduction patterns and desynchronized LV contractions by the RVa pacing increased the ELsys in the non-HCM group, which might be associated with future LV dysfunction represented as PICM.

4.3 | Mechanisms of the EL reduction by RVa pacing in the HCM group

The reduction in the vortex during the IVC period is thought to be one of the mechanisms of an increased ELsys in patients with HCM.[31-33] In patients with a normal systolic function, a large vortex during the IVC period contributes to an efficient blood flow and minimizes dissipative EL. HCM is characterized by myocardial disarray, fibrosis, and LV diastolic dysfunction.[16,17] Several recent studies have shown that a lower flow velocity is observed at the end of a rapid filling in HCM patients as compared to normal hearts because the inflow is limited during early diastole as a result of diastolic dysfunction.[31-33] At the end of a rapid filling, lower blood flow does not contribute to the formation of a large vortex during the IVC period in patients with HCM. Therefore, more energy is dissipated to achieve an efficient ejection, which results in an increased ELsys in patients with HCM.[31] It was also reported that the vortex area during the IVC period was significantly smaller in patients with HCM than in those with normal hearts.[31] Similar tendencies were observed in this study. RVa pacing enlarged and normalized the vortex during the IVC period in the HCM group (Figure 2), suggesting that RVa pacing improved the LV flow patterns and reduced the EL. Historically, RVa pacing has played an important role in the reduction of an LVOT obstruction.[34] A reduced contraction of the LV, paradoxical septal motion with a delayed septal thickening, limitation of an abnormal mitral valve motion, interaction with LV filling, and ventricular remodeling are considered the mechanisms of the reduction in the LVOT obstruction by RVa pacing.[6,35] From the results of this study, not only the aforementioned mechanisms, but a normalized flow vortex and reduced EL by RVa pacing were an additional mechanism of improving the hemodynamics in patients with HOCM.

Several studies have shown that RVa pacing does not change or rather exacerbates the diastolic function.[36-38] Therefore, the reason why the vortex was improved by RVa pacing in the HCM group was not thought to be an improvement in the diastolic function. Pak et al reported that RVa pacing increased the end-systolic volume and reduced the apical cavity

compression in patients with HCM and hypertensive heart disease.[36] In such patients, an increased end-systolic volume may preserve the cardiac cavity during diastole, creating large vortices. Therefore, a possible mechanism would be an enlargement of the vortex during the IVC period by an increased end-systolic volume. However, the left ventricular end-systolic dimension, left ventricular end-diastolic dimension, and LVEF between the AAI and DDD modes were not significantly different in this study. That might be because the number of patients was small, but it was not thought to be the main mechanism of those findings.

As a fact, the formation of the vortex was basically impaired in the HCM group, and the RVa pacing normalized the vortex, which decreased the ELsys and improved the flow dynamics in the HCM group, despite the EL having had increased in the non-HCM group in this study. Somehow there could be other factors that improve the EL by RVa pacing. To best of our knowledge, there have been no reports that have clarified this mechanism, so these might be novel findings.

5 | LIMITATIONS

This study had several limitations. First, this was a small-sized study conducted at a single center. All the non-HCM patients were inpatients with new device implantation. On the other hands, most of the HCM patients were outpatients, posing a selection bias, however, echocardiography was performed under stable condition even in the inpatients. Further, all patients in the HCM group had a preserved intrinsic AV conduction; however, low frequent RV pacing was observed (the RV pacing rate was 17.6 ± 26.7%) with a duration of 2262 ± 1448 days from the device implantation to the echocardiography. These factors might have affected the results. Second, the VFM was based on the two-dimensional continuity equation on the color Doppler image, and a highly distorted three-dimensional (3D) flow was not suitable for the VFM analysis, although a 3D evaluation may have allowed us to evaluate more precise information. Magnetic resonance imaging was applicable for the 3D evaluation, but it was restricted in the patients with device implantation. Third, the Nyquist limit may have affected the results of the flow analyses. Highly aliased color flow mapping may not have been corrected by VFM, although the aliasing flow was manually corrected. Only the early effects were evaluated in this study; therefore, the effect of the EL by RVa pacing on the long-term clinical events such as heart failure, LV dysfunction, and arrhythmic events was not evaluated. Further the clinical significance of the decrease in the EL with RVa pacing in hypertrophic nonobstructive cardiomyopathy (HNOCM) is unclear as of yet; therefore, future investigations with longer-term follow-ups are needed to confirm the prognostic value of the EL decrease with RVa pacing in HNOCM.

6 | CONCLUSIONS

In the vector flow mapping analysis, right ventricular apical pacing increased the mean systolic energy loss in patients without hypertrophic cardiomyopathy. Conversely, right ventricular pacing decreased the mean systolic energy loss and mean energy loss in one cardiac cycle in hypertrophic cardiomyopathy. The vector flow mapping analysis elucidated the impact of right ventricular apical pacing in the patients with hypertrophic cardiomyopathy.

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CONFLICTS OF INTEREST

The authors declares that there are no conflicts of interest related to this study.

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