



# Radiofrequency catheter ablation for improving myocardial work in patients with ventricular pre-excitation

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**Background:** Previous studies have not consistently found significant improvements in left ventricular ejection fraction or global longitudinal strain (GLS) after radiofrequency catheter ablation (RFCA) in patients with ventricular pre-excitation. The aim of this study was thus to explore the effects of RFCA on left ventricular function in patients with ventricular pre-excitation using a new noninvasive echocardiographic method of myocardial work.

**Methods:** A total of 34 patients with ventricular pre-excitation who underwent RFCA and 18 healthy controls were prospectively included in this study. Before and after participants underwent RFCA, electrocardiographic and echocardiographic data of the patients were collected at resting and pacing heart rates (HRs) of 100 beats per minute (bpm) and 120 bpm (controlled by high right atrial pacing during the procedure). Clinical data of the healthy controls at resting HR were also collected. A self-controlled paired sample *t* test was used to compare the differences before and after participants underwent RFCA.

**Results:** After participants underwent RFCA, the global wasted work (GWW) of the included patients decreased (resting HR: 165.3±68.8 *vs.* 92.6±42.5 mmHg%, *P*<0.001; HR of 100 bpm: 276.3±121.2 *vs.* 187.9±96.0 mmHg%, *P*<0.001; HR of 120 bpm: 323.9±126.7 *vs.* 181.0±74.3 mmHg%, *P*<0.001), while the global work efficiency (GWE) increased (resting HR: 91.5%±3.8% *vs.* 94.9%±1.6%; *P*<0.001; HR of 100 bpm: 87.0%±5.2% *vs.* 91.0%±3.3%, *P*<0.001; HR of 120 bpm: 85.0%±5.1% *vs.* 90.3%±3.7%, *P*<0.001).

**Conclusions:** In patients with ventricular pre-excitation, impaired GWW and GWE can be improved with RFCA. In clinical practice, noninvasive myocardial work assessment can be used in patients with ventricular pre-excitation.

**Keywords:** Ventricular pre-excitation; delta wave; echocardiography; myocardial work; radiofrequency catheter ablation

Submitted Sep 04, 2022. Accepted for publication Feb 13, 2023. Published online Mar 22, 2023.

doi: 10.21037/qims-22-925

View this article at: <https://dx.doi.org/10.21037/qims-22-925>

## Introduction

Ventricular pre-excitation refers to the early activation of the partial ventricular myocardium due to the rapid electrical conduction of sinus or atrial pulses through atrioventricular accessory pathways (AVAPs), resulting in a characteristic delta wave on an electrocardiogram (ECG) (1). In the general population, the detection rate of ventricular pre-excitation on ECG is 0.1–0.3%, and atrioventricular reentrant tachycardia is the most common arrhythmia (1). Radiofrequency catheter ablation (RFCA) is the first-line treatment for symptomatic patients to alleviate their complaints and prevent life-threatening arrhythmias, including pre-excited atrial fibrillation and ventricular fibrillation (1). It is essential to accurately evaluate the left ventricular (LV) function in everyday clinical practice.

Over the past decade, the conventional echocardiographic parameter of left ventricular ejection fraction (LVEF) and speckle-tracking echocardiography (STE) have been used to assess the effect of RFCA of the AVAP(s) on LV function. However, previous studies have not consistently reported significant improvements in LV function after RFCA in patients with ventricular pre-excitation. For example, in the study of Tomaske *et al.* (2), impaired LVEF of patients with right-sided AVAP(s) improved significantly after participants underwent RFCA. In contrast, Nagai *et al.* (3) found that the global longitudinal strain (GLS) did not improve remarkably after participants underwent RFCA. Similarly, Dai *et al.* (4) did not report improvement in the LVEF in patients with left-sided AVAP(s) after RFCA. One explanation for these varied results may be that conventional parameters and STE are not sufficiently sensitive to reflect the myocardial dysfunction in patients with ventricular pre-excitation.

Myocardial work is an alternative tool for studying LV function through incorporating deformation and LV pressure into its analysis (5). A growing amount of evidence supports the use of myocardial work to detect early-stage heart diseases, aid prognostication, and predict therapeutic responses (6–14). However, myocardial work has not been studied in a ventricular pre-excitation setting.

Therefore, the aim of this study was to explore the effects of RFCA on myocardial work parameters in patients with pre-excitation. We present the following article in accordance with the STROBE reporting checklist (available at <https://qims.amegroups.com/article/view/10.21037/qims-22-925/rc>).

## Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Institution Review Board of Sun Yat-Sen Memorial Hospital. Written informed consent was obtained from all the participants.

### *Patients and study protocol*

Patients with delta waves characteristic of ventricular pre-excitation on a 12-lead ECG who sought medical advice at Sun Yat-Sen Memorial Hospital from May 1, 2020, to August 20, 2021, were prospectively recruited into this study. Patients with structural heart disease, coronary heart disease, cardiac conduction defects, frequent premature ventricular contractions, hyperthyroidism, hypothyroidism, or poor-quality echocardiography were excluded.

All patients underwent electrocardiographic and echocardiographic examinations before and after undergoing RFCA at different heart rates (HRs). The HRs were resting HR, 100 bpm, and 120 bpm as controlled by high right atrium (HRA) pacing (described in detail in the following section). At the resting HR, images were collected within 24 hours before RFCA and again within 48 hours after RFCA. At pacing HRs, electrocardiographic and echocardiographic examinations were performed within 15 minutes before and after the ablation of the AVAP(s).

If the delta wave on the ECG at the resting HR was not detected (intermittent pre-excitation) but was demonstrated at pacing HRs before RFCA, electrocardiographic and echocardiographic examinations were performed at pacing HRs. If the delta wave on the ECG disappeared or Wenckebach phenomenon occurred during pacing, electrocardiographic and echocardiographic examinations at pacing HRs were abandoned. Antiarrhythmic drugs were discontinued for at least 5 half-lives before participants underwent RFCA, and patients did not need to take antiarrhythmic drugs after successful RFCA according to the guidelines (1).

The control group consisted of 18 age- and gender-matched healthy individuals who came for a health screening and who had normal echocardiographic and electrocardiographic findings at rest. Those with cardiovascular diseases, cardiovascular medications, endocrine diseases (e.g., hyperthyroidism or hypothyroidism), and poor-quality echocardiography were excluded. Blood pressure, HR,

height, and weight were routinely collected in all participants.

### *Electrocardiography*

All patients underwent a 12-lead ECG during sinus rhythm using a Mac 5000 System (GE Healthcare) before and after RFCA. Measurements of delta and QRS intervals were performed using the system analysis of intervals.

### *Echocardiography*

Before and after RFCA at the 3 HRs, a transthoracic echocardiographic examination was performed using a GE Vivid E95 echo system with an M5Sc-D probe (GE Healthcare) by an experienced cardiologist who was blinded to the invasive electrophysiological study (EPS) findings. Images and data were analyzed offline using Echopac (version 204; GE Vingmed Ultrasound).

LVEF was calculated using the biplane Simpson method. Global and segmental longitudinal strain analyses were performed using STE (Echopac204, GE Vingmed Ultrasound). Segmental strains were obtained from apical 2-, 3, and 4-chamber views. Mitral, aortic, and pulmonary valve antegrade flow Doppler spectra were measured. The standard deviation (SD) of the time-to-peak longitudinal strain for all segments, ie, peak strain dispersion (PSD) was measured (12).

Measurement of myocardial work was assessed using the method introduced and validated by Russell *et al.* (15). Myocardial work was analyzed using Echopac (version 204; GE Vingmed Ultrasound) after the calculations of LV GLS and peak noninvasive systolic blood pressure were input. Pressure-strain loops were synchronized with the opening and closing times of the aortic and mitral valves. Myocardial work was quantified by calculating the rate of regional shortening by differentiating the strain tracing and multiplying the result by instantaneous LV pressure integrated over time. During the LV ejection time, the work efficiency of the LV segments was analyzed, and the average of all segmental values was considered the global value. The following parameters were acquired using Echopac 204 software: the global work index (GWI; mmHg%), which represented the area within the LV pressure-strain loop; the global constructive work (GCW; mmHg%), which represented the LV work generated by shortening of the myocardium during systole and lengthening within isovolumetric relaxation; the global wasted work (GWW; mmHg%), which was the amount of ineffective energy with LV lengthening during systole and

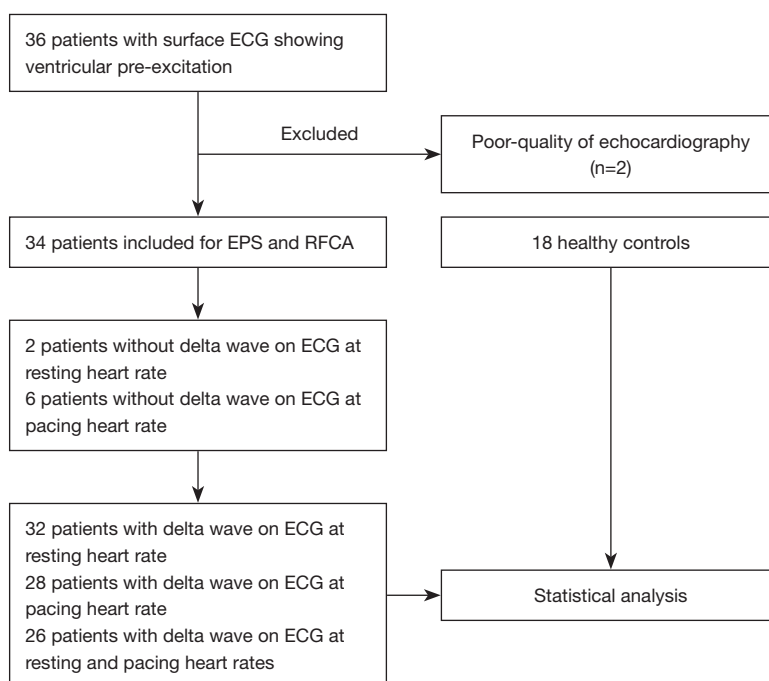
shortening during isovolumetric relaxation; and the global work efficiency (GWE; %), which was calculated as  $GCW / (GCW + GWW)$ .

### *Electrophysiological studies and radiofrequency catheter ablation*

According to the guidelines (1), an EPS was applied to symptomatic individuals and asymptomatic patients who had high-risk occupations or hobbies, including drivers, pilots, and competitive athletes (class I of recommendation, level B of evidence). A quadripolar electrode catheter was inserted percutaneously and advanced to the right atrium, right ventricular apex, or His bundle position as appropriate. A decapolar catheter was advanced into the coronary sinus. The location of each AVAP was confirmed using standard electrophysiological maneuvers. Programmed atrial stimulation was used to evaluate the AVAP antegrade effective refractory period (APERP). This was completed using atrium pacing close to the AVAP atrial insertion site to obviate the effect of intra-atrial conduction delay. Before RFCA was conducted, electrocardiographic and echocardiographic examinations were performed using HRA overdrive pacing at cycle lengths of 600 ms and 500 ms at HRs of 100 bpm and 120 bpm, respectively, with a 1:1 conduction over the AVAP(s). RFCA was then performed in symptomatic patients (class I of recommendation, level B of evidence) (1). For asymptomatic patients, if AVAP with high-risk properties [APERP  $\leq$ 250 ms, shortest pre-excited RR interval during atrial fibrillation (SPERRI)  $\leq$ 250 ms, multiple AVAPs, or an inducible AP-mediated tachycardia] was confirmed with EPS, RFCA was performed according to the relevant guidelines (class I of recommendation, level B of evidence) (1). The end point of RFCA was a complete bidirectional block of AVAP conduction. After participants underwent RFCA, the cardiac conduction system was evaluated again to determine whether supraventricular tachyarrhythmia was still inducible and whether there was residual conduction of AVAP(s). Subsequently, electrocardiographic and echocardiographic examinations were performed at HRs of 100 bpm and 120 bpm with HRA pacing.

### *Sample size estimation*

The study was a self-pair design study investigating the effect of RFCA on myocardial work parameters in patients with ventricular pre-excitation. The GWE of the study participants was observed recorded. Based on pre-



**Figure 1** Flowchart of participant selection. ECG, electrocardiogram; EPS, electrophysiological study; RFCA, radiofrequency catheter ablation.

experiments, the mean GWE before participants underwent RFCA was expected to be 91%. After participants underwent RFCA, the GWE was expected to be elevated by 4% with an estimated SD of the difference of 4.8%, setting the bilateral  $\alpha$  at 0.05 and the certainty at 90%. The sample size of 20 cases for the patient group and 15 cases for the control group was calculated using PASS 15 software (NCSS LLC).

### Statistical analysis

Numerical data are presented as mean  $\pm$  SD for continuous variables and as numbers and percentages for categorical variables.

Comparisons of parameters among different HRs of the same individual before participants underwent RFCA were evaluated using the paired samples  $t$  test. A  $P$  value  $<0.01$  was considered statistically significant ( $\alpha=0.05$  divided by the number of multiple comparisons).

Differences between the pre- and post-RFCA parameters of the same individual were assessed using a paired samples  $t$  test. A  $P$  value  $<0.05$  was considered statistically significant.

Differences between 2 groups were compared using the Student  $t$  test. Comparisons between more than 2 groups were conducted with 1-way analysis of variance (ANOVA),

and a  $P$  value  $<0.05$  was considered statistically significant. Multiple comparisons with Bonferroni adjustment ( $\alpha=0.05$  divided by the number of multiple comparisons) were conducted if there was significance in the ANOVA.

Data were analyzed using SPSS 25.0 (IBM Corp.).

### Intra- and interobserver variability

Echocardiograms of 12 patients were randomly selected to assess reproducibility. A second physician who was blinded to patients' clinical data and the other's results, performed independent measurements of the echocardiographic data. Of the 2 observers, 1 blindly analyzed the same echocardiograms a second time. Intra- and interobserver variability was calculated using intraclass correlation coefficients (ICCs) and the standard error of measurement (SEM).

## Results

### Clinical characteristics

The study flowchart is shown in *Figure 1*. Among the 36 patients with ECG who showed ventricular pre-excitation, 2 were excluded because of poor-quality echocardiography.

**Table 1** Baseline clinical characteristics of patients with ventricular pre-excitation and healthy controls

Characteristics	Patients (n=34)	Controls (n=18)	P value
Averaged age, years	40.44±16.30	42.50±15.51	0.73
Height, cm	163.91±9.86	162.94±8.76	0.38
Weight, kg	59.62±9.45	62.33±8.51	0.58
Female patients, n (%)	14 (41.2)	9 (50.0)	0.69
HR, bpm	73.72±10.74 (n=32) <sup>a</sup>	73.17±9.67	0.91
SBP, mmHg	121.34±13.34	118.50±11.56	0.87
DBP, mmHg	74.28±9.94	74.44±8.70	0.98
QRSd, ms	130.22±15.12 (n=32) <sup>a</sup>	84.33±10.98	0.05
PSD, ms	53.54±25.75 (n=32) <sup>a</sup>	48.56±10.20	0.10
LVEF, %	60.19±7.63 (n=32) <sup>a</sup>	62.06±5.22	0.07
GLS, %	-18.59±2.59 (n=32) <sup>a</sup>	-19.42±1.66	0.10
GWI, mmHg%	1,783.62±337.14 (n=32) <sup>a</sup>	1,838.44±324.10	0.49
GCW, mmHg%	2,029.23±313.48 (n=32) <sup>a</sup>	2,128.33±330.87	0.65
GWW, mmHg%	165.28±68.82 (n=32) <sup>a</sup>	94.83±33.39	0.03*
GWE, %	91.49±3.82 (n=32) <sup>a</sup>	94.78±1.63	0.03*
APERP, ms (n=26)	305.19±80.64	-	-
Location of AVAP, n (%)			
Left free wall	18 (53.0)	-	-
Septum	8 (23.5)	-	-
Right free wall	8 (23.5)	-	-
Multiple AVAPs, n (%)	2 (5.9)	-	-
Intermittent pre-excitation, n (%) <sup>a</sup>	2 (5.9)	-	-
Wenckebach phenomenon, n (%) <sup>b</sup>	2 (5.9)	-	-
Disappearance of delta wave, n (%) <sup>c</sup>	4 (11.8)	-	-
Asymptomatic, n (%)	7 (20.6)	-	-
RFCA success, n (%)	34 (100.0)	-	-

Data are expressed as mean ± standard deviation (SD). <sup>a</sup>, Delta wave on electrocardiogram was not detected at resting heart rate. <sup>b</sup>, Wenckebach phenomenon occurred at pacing heart rates. <sup>c</sup>, Delta wave on electrocardiogram disappeared because atrial pulses did not conduct through Accessory pathway at pacing heart rates. \*P<0.05. HR, heart rate; bpm, beat per minute; QRSd, QRS wave duration; PSD, peak strain dispersion LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; AVAP, atrioventricular accessory pathway; APERP, accessory pathway effective refractory period; RFCA, radiofrequency catheter ablation.

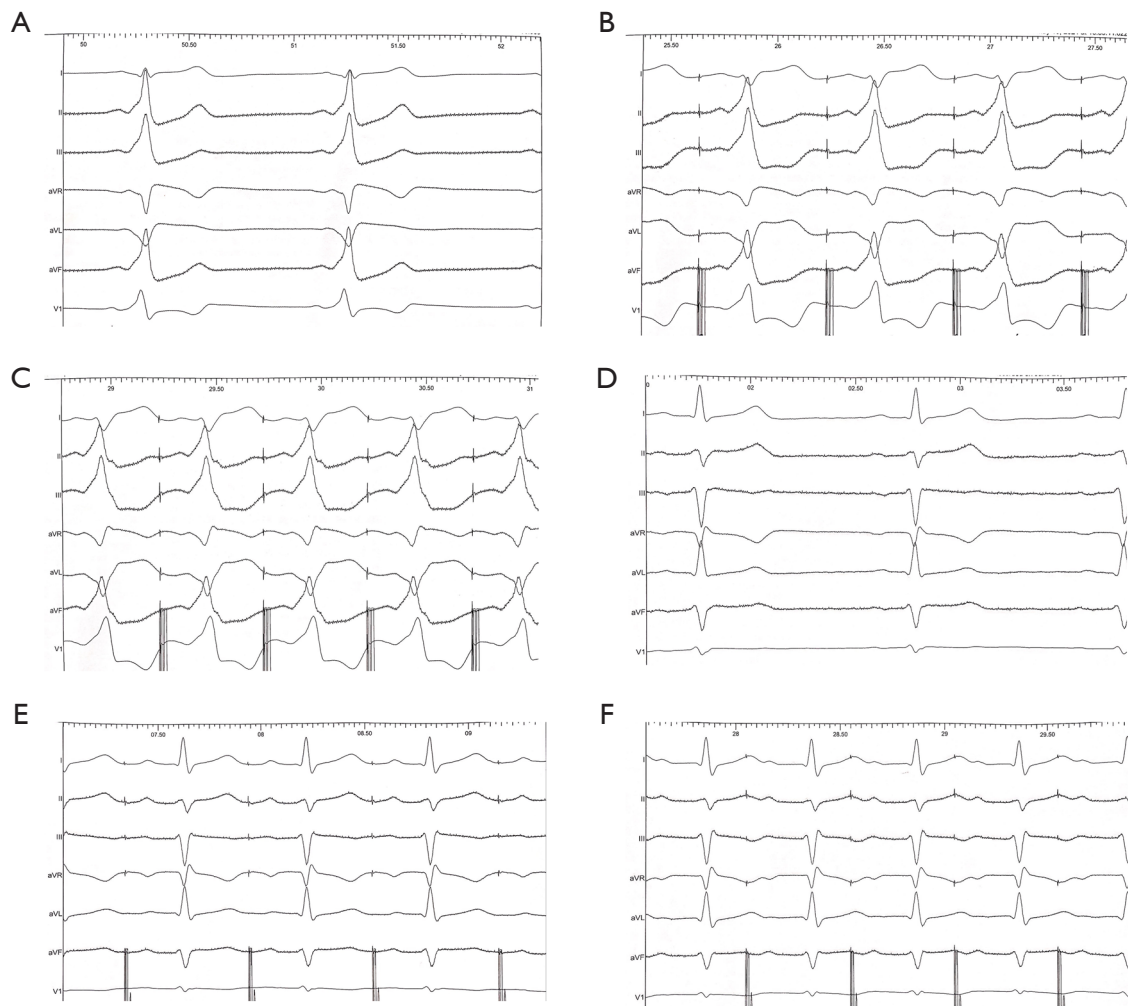
Thus, 34 patients were verified as having ventricular pre-excitation by AVAP(s), and their electrocardiographic and echocardiographic data were collected.

The baseline clinical characteristics and electrophysiological characteristics of these patients and the 18 healthy controls are

presented in *Table 1*. All RFCA procedures were performed without complications.

Among the 34 patients, 32 patients underwent electrocardiographic and echocardiographic examinations at resting HR because 2 patients were diagnosed with





**Figure 2** A surface electrocardiogram of a patient with a left free-wall accessory pathway located at the 2 to 3 o'clock position of the mitral annulus at resting heart rate (A, D), heart rate of 100 bpm (B, E), and heart rate of 120 bpm (C, F). Images A-C and D-F were acquired before and after participants underwent RFCA, respectively. Before RFCA, as the heart rate increased, the delta wave widened (58 ms, 62 ms, and 64 ms at resting heart rate, heart rate of 100 bpm, and 120 bpm, respectively), and the QRS wave broadened (146 ms, 174 ms, and 184 ms at resting heart rate, heart rate of 100 bpm, and 120 bpm, respectively; A-C). After RFCA, the delta wave disappeared, and the QRS wave narrowed (80 ms, 82 ms, and 78 ms at resting heart rate, heart rate of 100 bpm, and 120 bpm, respectively) at each heart rate (D-F).

intermittent pre-excitation without a delta wave on the ECG at resting HR before undergoing RFCA. A total of 28 patients accepted electrocardiographic and echocardiographic examinations at pacing HRs because 6 patients experienced the disappearance of the delta wave or Wenckebach phenomenon during pacing. In total, 26 patients underwent electrocardiographic and echocardiographic examinations at resting HR and pacing HRs.

#### *Electrocardiographic and echocardiographic data of patients pre-RFCA at different heart rates*

As presented in *Figure 2*, the degree of ventricular pre-excitation increased with an increasing HR, as evidenced by the widening of the delta wave on the surface ECG. Electrocardiographic and echocardiographic data at different HRs before RFCA are shown in *Table 2*. As the

**Table 2** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation at different heart rates pre-RFCA (n=26)

Items	Resting HR (73±9 bpm)	HR =100 bpm	HR =120 bpm	P <sup>a</sup>	P <sup>b</sup>	P <sup>c</sup>
Delta, ms	46.4±7.7	51.0±10.0	53.9±10.3	0.001*	0.02	0.001*
QRSd, ms	129.1±16.4	137.0±21.7	144.3±23.7	0.01*	0.001*	<0.001*
PSD, ms	53.6±28.4	57.2±21.7	59.6±19.2	0.45	0.53	0.24
LVEF, %	59.2±7.5	53.9±7.1	52.0±7.3	0.002*	0.13	<0.001*
GLS, %	-18.7±2.4	-16.4±2.4	-15.0±2.5	<0.001*	<0.001*	<0.001*
GWI, mmHg%	1,809.2±334.7	1,827.4±446.5	1,547.7±471.2	0.79	0.001*	<0.001*
GCW, mmHg%	2,053.4±309.0	2,228.1±446.3	2,117.7±385.4	0.03	0.07	0.39
GWW, mmHg%	166.7±74.2	279.6±121.9	322.9±118.2	<0.001*	0.005*	<0.001*
GWE, %	91.5±4.1	86.9±5.4	84.7±5.1	<0.001*	0.001*	<0.001*
SBP, mmHg	123.2±13.2	140.1±19.8	139.3±18.4	<0.001*	0.66	<0.001*
DBP, mmHg	75.8±10.2	88.8±14.8	92.2±17.4	<0.001*	0.03	<0.001*

Comparisons within the same individual were performed using a paired-samples *t* test. Data are expressed as mean ± SD. <sup>a</sup>, HR =100 bpm vs. resting heart rate; <sup>b</sup>, HR =120 bpm vs. HR =100 bpm; <sup>c</sup>, HR =120 bpm vs. resting heart rate. \*P<0.01. QRSd, QRS wave duration; PSD, peak strain dispersion; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.

HR increased, the delta wave and QRS wave widened, LVEF became impaired, GLS worsened, GWW increased, and GWE worsened (Figure 3).

#### **Electrocardiographic and echocardiographic data of patients pre- and post-RFCA**

Electrocardiographic and echocardiographic data before and after participants underwent RFCA are shown in Table 3. QRS wave duration shortened remarkably after participants underwent RFCA at the 3 distinct HRs (all P values <0.05). There was no significant enhancement of LVEF after ablation at the 3 HRs, and GLS improved significantly after RFCA only at the HR of 120 bpm (P<0.02). As for myocardial work parameters, compared to those acquired before RFCA, GWW decreased significantly at the different HRs (resting HR: 165.3±68.8 vs. 92.6±42.5 mmHg%, P<0.001; HR of 100 bpm: 276.3±121.2 vs. 187.9±96.0 mmHg%, P<0.001; HR of 120 bpm: 323.9±126.7 vs. 181.0±74.3 mmHg%, P<0.001), while GWE increased remarkably (resting HR: 91.5%±3.8% vs. 94.9%±1.6%, P<0.001; HR of 100 bpm: 87.0%±5.2% vs. 91.0%±3.3%, P<0.001; HR of 120 bpm: 85.0%±5.1% vs. 90.3%±3.7%, P<0.001). The distribution of myocardial work at the 3 HRs was more homogenous after participants

underwent RFCA (Figures 4–6).

#### **Electrocardiographic and echocardiographic data in patients with different locations of AVAP**

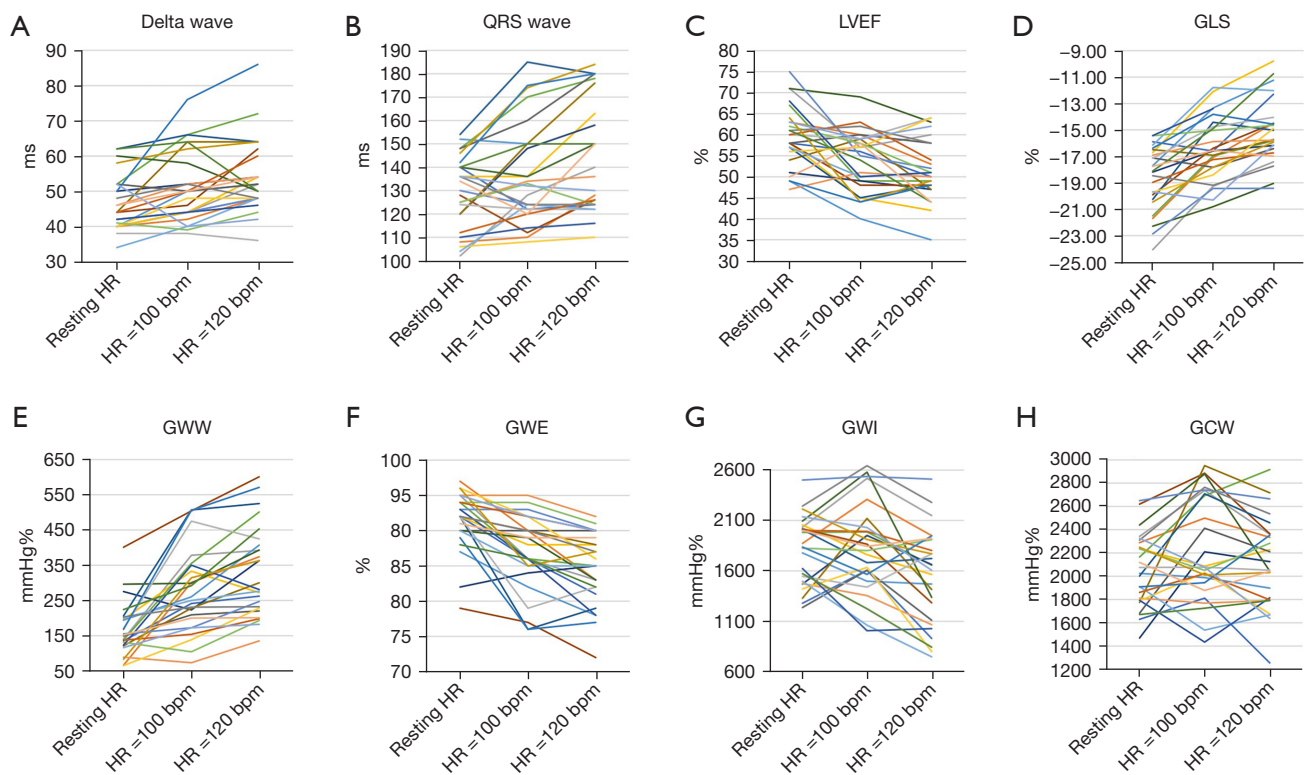
Only GWE at resting HR of the left free-wall AVAP group and that of the septal AVAP group before RFCA showed statistical differences (92.8%±2.5% vs. 88.1%±5.9%; P<0.01; Tables S1–S3).

#### **Electrocardiographic and echocardiographic data in asymptomatic and symptomatic patients**

For myocardial work parameters, the differences in the change in GWW/GWE before and after RFCA was not statistically significant in either group (Tables S4–S6).

#### **Electrocardiographic and echocardiographic data in patients and healthy controls at resting HR**

Compared to the healthy control group, patients with ventricular pre-excitation had worse GWW and GWE before RFCA, but these differences disappeared after RFCA (Table S7).



**Figure 3** Graphs showing the changes at different heart rates in some electrocardiographic and echocardiographic indices of the 26 enrolled patients (pre-RFCA). As the heart rate increased, the delta wave (A) and QRS wave (B) widened, LVEF (C) and GLS (D) worsened, GWW (E) increased, and GWE (F) decreased. However, GWI (G) and GCW (H) did not show a discernible trend with increasing heart rate. RFCA, radiofrequency catheter ablation; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWW, global waste work; GWE, global work efficiency; GWI, global work index; GCW, global constructive work.

### *Change in GWW/GWE according to HR increase in the patients*

Before RFCA, the difference in GWW/GWE between the the 100 bpm HR group and resting HR group ( $\delta_1$ ) and between the 120 bpm HR group and the 100 bpm HR group ( $\delta_2$ ) were not statistically significant. However, the difference in GWW/GWE between  $\delta_1$  and  $\delta_2$  was remarkable after RFCA. Only the change in  $\delta_2$  of GWW before and after RFCA was statistically different (Tables S8,S9).

### *Intra- and interobserver variability*

The assessment of noninvasive myocardial work and GLS exhibited excellent reproducibility (Table 4). The ICC for the interobserver assessment was excellent for GWI (95% CI: 0.873–0.990), GCW (95% CI: 0.806–0.985), GWW (95% CI: 0.824–0.985), GWE (95% CI: 0.827–0.985), and GLS (95% CI: 0.733–0.977). Similarly, the ICC for

intraobserver assessment was excellent for GWI (95% CI: 0.885–0.991), GCW (95% CI: 0.833–0.987), GWW (95% CI: 0.892–0.992), GWE (95% CI: 0.845–0.987), and GLS (95% CI: 0.846–0.987).

## **Discussion**

Ventricular pre-excitation is characterized by the advancement of certain LV segmental contractions due to the early electrical conduction through AVAP(s). Thus, evaluation of LV function is integral to the clinical practice of cardiology.

### *Myocardial work in patients with ventricular pre-excitation*

Improvements in LV function according to LVEF or GLS after RFCA are not consistently apparent in previous



**Table 3** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation at different heart rates pre- and post-RFCA

Items	Resting heart rate (n=32)			HR =100 bpm (n=28)			HR =120 bpm (n=28)		
	Pre-RFCA	Post-RFCA	P value	Pre-RFCA	Post-RFCA	P value	Pre-RFCA	Post-RFCA	P value
Delta, ms	47.1±8.7	–	–	50.6±9.8	–	–	53.5±10.1	–	–
QRSd, ms	130.2±15.1	82.6±10.0	<0.001*	136.6±20.9	82.6±10.5	<0.001*	143.4±23.1	81.5±11.1	<0.001*
PSD, ms	53.5±25.8	46.1±13.6	0.13	56.1±21.5	50.5±13.5	0.10	59.7±18.5	47.9±14.8	0.008*
LVEF, %	60.2±7.6	61.4±6.4	0.21	54.0±7.2	55.5±5.9	0.05	51.4±7.2	53.3±7.0	0.10
GLS, %	–18.6±2.6	–18.9±2.2	0.38	–16.5±2.5	–16.6±2.2	0.66	–15.0±2.5	–15.9±2.3	0.02*
GWI, mmHg%	1,783.6±337.1	1,780.8±284.0	0.94	1,820.4±454.1	1,835.6±406.9	0.80	1,548.6±474.8	1,541.5±455.2	0.90
GCW, mmHg%	2,029.2±313.5	2,024.2±291.5	0.90	2,203.8±460.9	2,174.9±388.3	0.63	2,112.6±386.4	2,047.3±397.4	0.27
GWW, mmHg%	165.3±68.8	92.6±42.5	<0.001*	276.3±121.2	187.9±96.0	<0.001*	323.9±126.7	181.0±74.3	<0.001*
GWE, %	91.5±3.8	94.9±1.6	<0.001*	87.0±5.2	91.0±3.3	<0.001*	85.0±5.1	90.3±3.7	<0.001*
HR, bpm	73.7±10.7	74.0±12.5	0.82	100	100	–	120	120	–
SBP, mmHg	121.3±13.3	118.0±11.0	0.003*	139.0±19.8	138.4±18.3	0.65	138.1±18.4	136.7±17.9	0.34
DBP, mmHg	74.3±9.9	73.1±6.4	0.33	88.1±14.5	88.5±15.5	0.75	91.7±17.1	91.3±15.7	0.70

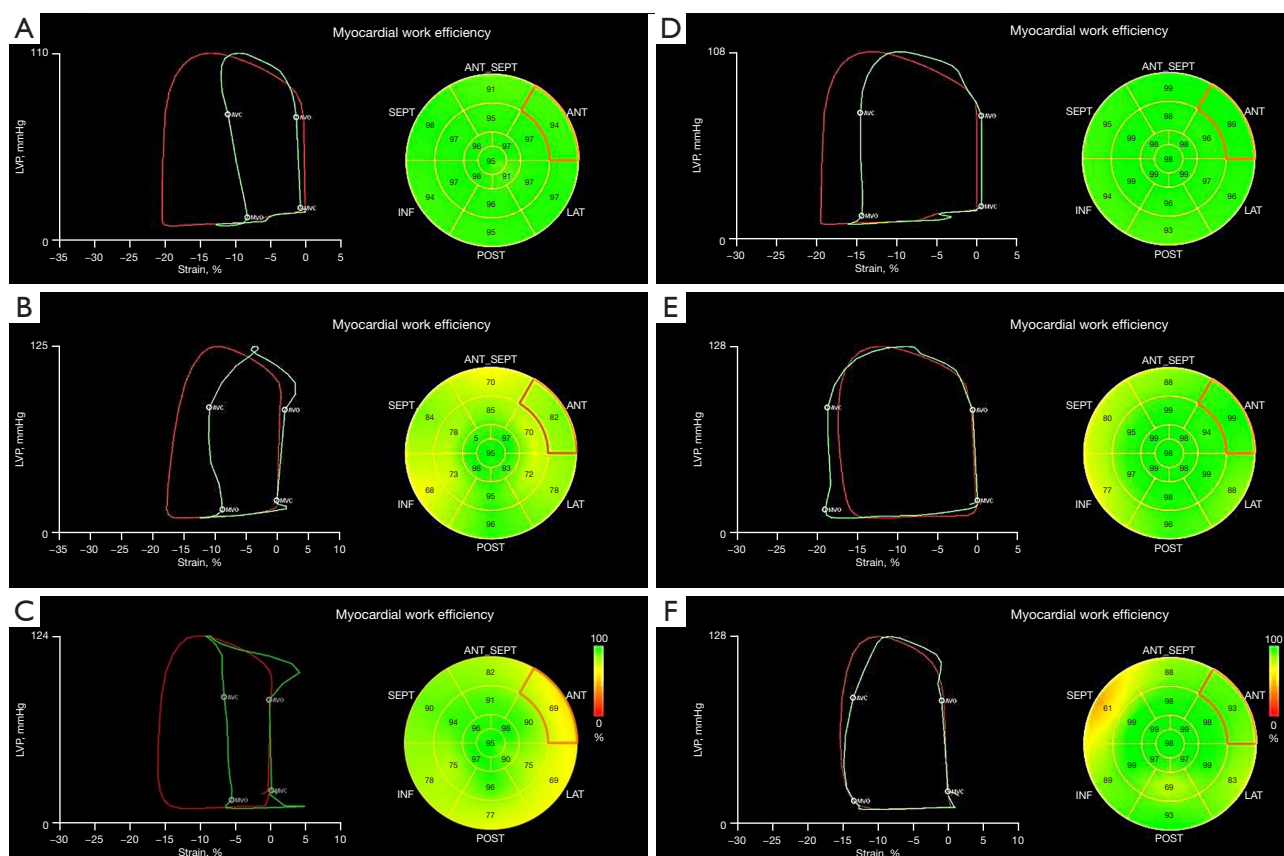
Comparisons within the same individual were performed using a paired-samples *t* test. Data are expressed as mean ± SD. \*P<0.05. QRSd, QRS wave duration; PSD, peak strain dispersion; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.

studies on ventricular pre-excitation (3,4) nor were they in our study. A possible explanation for this finding is that conventional indicators are not sufficiently sensitive to reflect the underlying myocardial dysfunction. LVEF provides important information about LV function by measuring changes in LV volume, which may be less apparent in patients with ventricular pre-excitation. Many studies have confirmed that the deformation parameter GLS surpasses LVEF in its ability to detect disease in the early stage (16–21), but its load dependency may lead to misinterpretation of the actual myocardial function.

Recently, the noninvasive echocardiographic method of myocardial work introduced by Russell *et al.* (15) has been investigated in various cardiovascular diseases. Myocardial work, as the combination of strain and after-load, is an alternative tool for studying LV function regionally and globally. Myocardial work may be a more comprehensive evaluation of LV function, as it incorporates systolic, diastolic, and isovolumic components (22). Synchronized myocardial contraction is essential for efficient LV ejection, which can be reduced by uncoordinated myocardial contractions. Noninvasive echocardiographic myocardial work can quantify the LV work consumed due to

dyssynchronous myocardial contractions.

Our data showed that before RFCA, the patients' GWW (165.3±68.8 mmHg%) was higher than that of the healthy control group (94.8±33.4 mmHg%) and the normal range (53–122.2 mmHg%) (23), while GWE (91.5±3.8%) was lower than that of the healthy control group (94.8±1.6 mmHg%) and the normal range (94–97%) (23). A possible reason for this phenomenon is that AVAP(s) might cause an LV dyssynchrony pattern. According to the definition of GWW by Russell *et al.* (15), inappropriate myocardial contraction and prolongation throughout the cardiac cycle lead to an increase in GWW. In ventricular pre-excitation with left-sided AVAP, rapid electrical impulses conducted through AVAP cause premature contraction of the LV myocardium inserted with AVAP. In ventricular pre-excitation with right-sided AVAP, complex electromechanical activity results in the premature contraction of a portion of the LV myocardium. In both cases, part of the LV myocardium contracts prematurely before mitral valve closure and then stretches during systole. In addition, other LV segments may also contract and prolong inappropriately due to the complex electromechanical activity. These eventually manifest as



**Figure 4** A bull's-eye depicting regional and global myocardial work efficiency and LV pressure-strain loop (LVPSL) in a patient with a left free-wall accessory pathway located at the 2 to 3 o'clock position of the mitral annulus at resting heart rate (A,D), heart rate of 100 bpm (B,E), and heart rate of 120 bpm (C,F). Images in the upper line (A-C) and the ones in the lower line (D-F) were acquired before and after participants underwent RFCA, respectively. At each heart rate, global myocardial work efficiency (GWE) and LVPSL were significantly improved after participants underwent RFCA. LV, left ventricle; RFCA, radiofrequency catheter ablation; bpm, beats per minute.

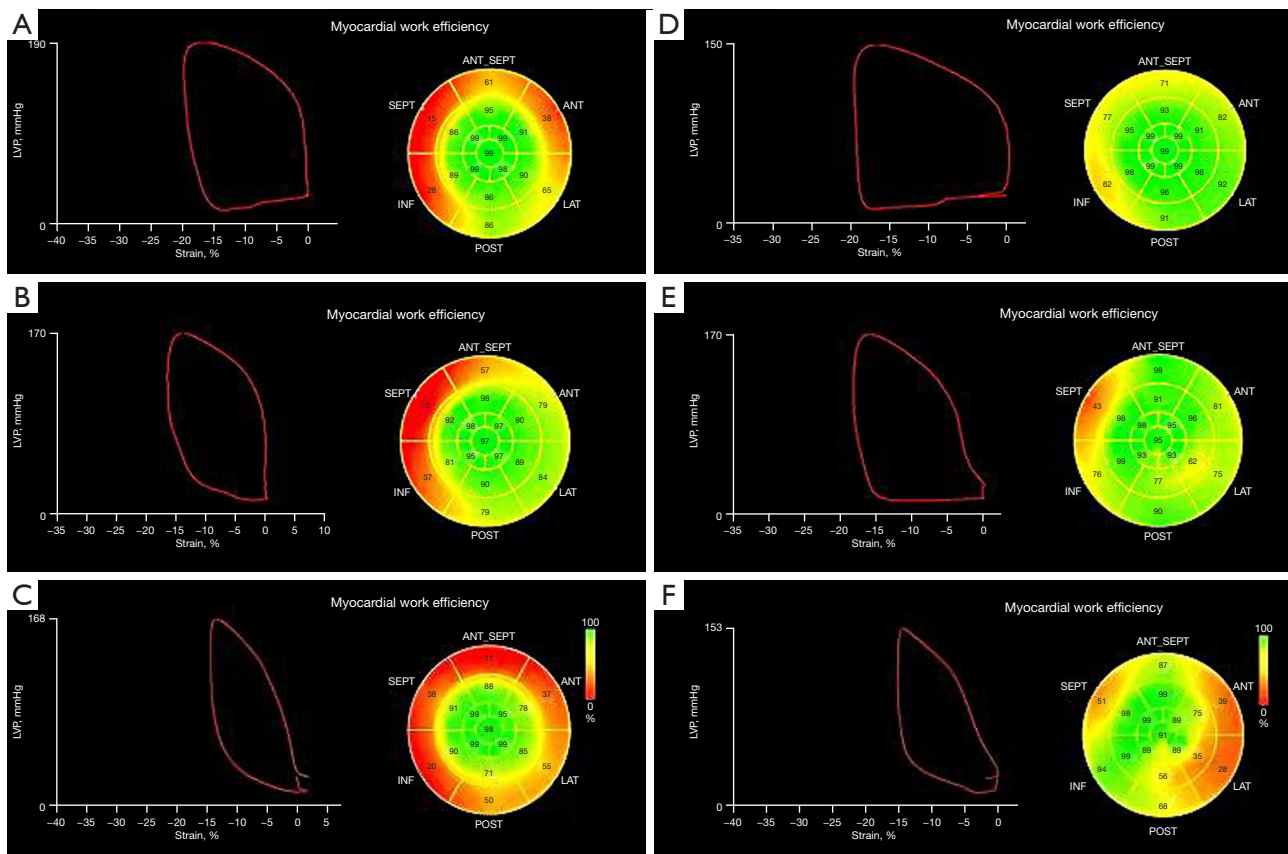
a disproportionate increase of GWW and GCW, which provoke a reduction of GWE.

In our study, the patients' LVEF and GLS were still within the normal range before RFCA, and their GWW and GWE were impaired, suggesting that the LV function of the patients with ventricular pre-excitation may have been in a "suboptimal" state. LV dysfunction in patients with ventricular pre-excitation is a growing concern. Apart from tachyarrhythmias, LV dyssynchrony caused by AVAP(s) is another mechanism that can lead to potential LV dysfunction in ventricular pre-excitation (1,24-26). Nagai *et al.* (3) attributed the improvement of LVEF to the resynchronization of LV contraction after AVAP ablation. Our data demonstrated that GWW and GWE improved significantly after participants underwent RFCA. This finding suggests that RFCA effectively improves LV

function in patients with ventricular pre-excitation, possibly by resynchronizing the LV contraction.

When we explored the effect of AVAP location on myocardial work parameters, our data showed that only GWE at resting HR was statistically different between the left free-wall AVAP group and the septal AVAP group. In addition, we observed that the change in GWE was greater in the left free-wall and septal AVAP groups as HR increased, suggesting that left free-wall and septal AVAP may have a greater effect on myocardial work parameters in patients with rapid HRs.

The comparison between symptomatic and asymptomatic patients showed that GWW/GWE improved after patients underwent RFCA in both groups, but the differences in change in GWW/GWE before and after RFCA were not statistically significant in either group. This



**Figure 5** A bull's-eye depicting regional and global myocardial work efficiency and LV pressure-strain loop (LVPSSL) in a patient with a septal accessory pathway at a resting heart rate (A,D), heart rate of 100 bpm (B,E), and heart rate of 120 bpm (C,F). Images in the upper line (A-C) and the ones in the lower line (D-F) were acquired before and after participants underwent RFCA, respectively. At each heart rate, global myocardial work efficiency (GWE) and LVPSSL were significantly improved after participants underwent RFCA. LV, left ventricle; RFCA, radiofrequency catheter ablation; bpm, beats per minute.

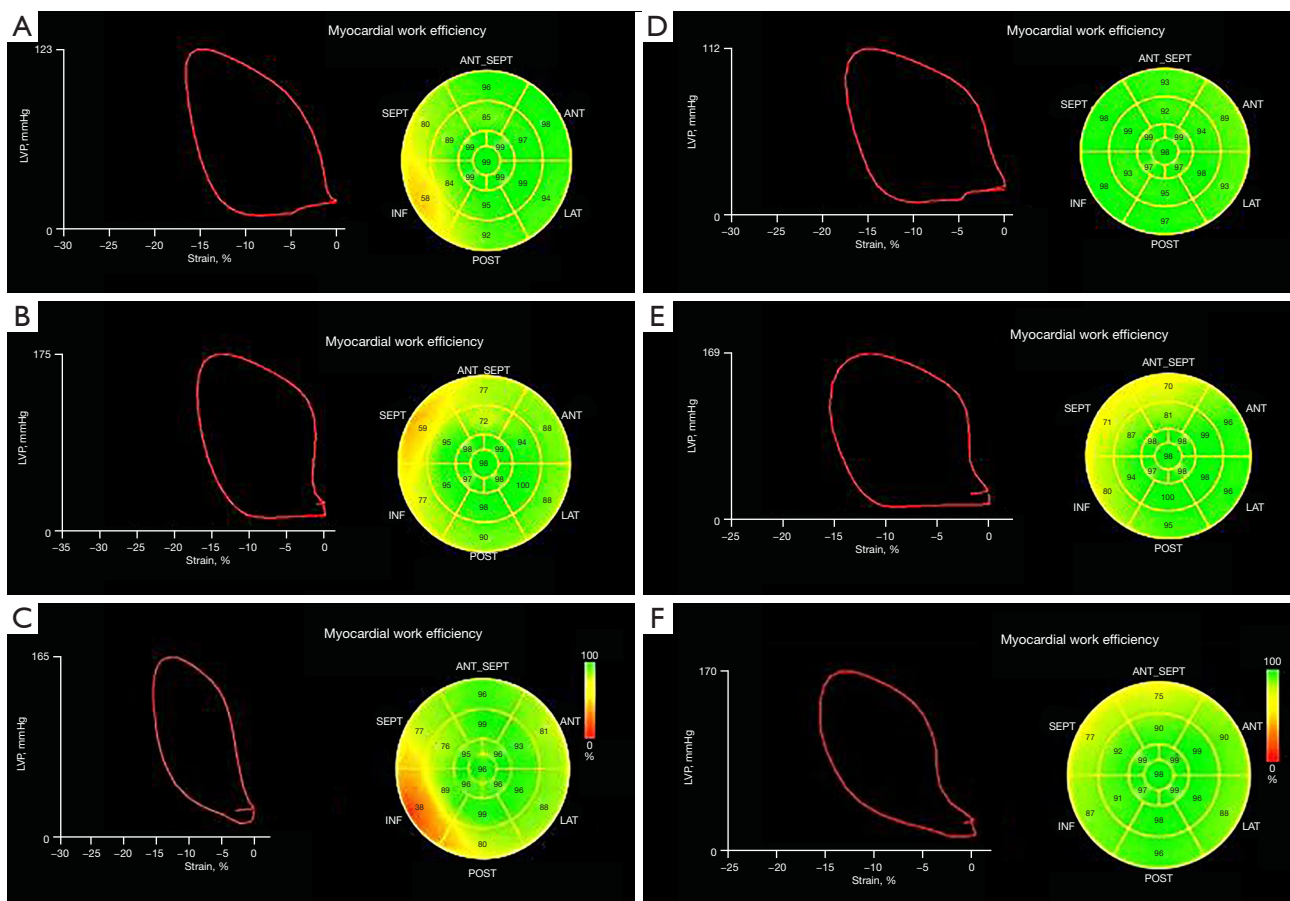
finding indicates that the effects of RFCA on improving myocardial work parameters are similar for asymptomatic and symptomatic patients.

#### ***Exercise intolerance in patients with ventricular pre-excitation***

In clinical practice, some patients with ventricular pre-excitation experience exertional dyspnea or impaired exercise tolerance. Cases of improvement of exercise intolerance after RFCA in patients with ventricular pre-excitation have also been reported (27-29). Using cardiopulmonary exercise testing, Książczyk *et al.* (30) demonstrated impaired physical performance in asymptomatic children with ventricular pre-excitation compared to matched healthy children ( $VO_{2max}$ :  $36.67 \pm 6.66$  vs.  $44.45 \pm 8.37$  mL/kg/min;  $P < 0.001$ ). Their

follow-up study identified improvement in the physical performance in children with ventricular pre-excitation (31). However, the recommendation of EPS and RFCA in these patients has not been proposed or unified.

In this study, we altered and controlled the heart rate of the patients by means of HRA pacing, which to some extent was able to simulate the sinus rhythm during exercise. Before RFCA, we found that as HR increased, GWW increased and GWE decreased, indicating LV insufficiency in patients with ventricular pre-excitation when they exercised. A possible explanation for this finding is that LV dyssynchrony is a dynamic condition, and its degree can be altered by exercise, as illustrated in previous studies on patients with ischemic cardiomyopathy (32-34). However, even the adverse effects observed at rapid HRs can be improved by successful RFCA.



**Figure 6** A bull's-eye depicting regional and global myocardial work efficiency and LV pressure-strain loop (LVPSL) in a patient with a right free-wall accessory pathway at a resting heart rate (A,D), heart rate of 100 bpm (B,E), and heart rate of 120 bpm (C,F). Images in the upper line (A,B,C) and the ones in the lower line (D,E,F) were acquired before and after participants underwent RFCA, respectively. At each heart rate, global myocardial work efficiency (GWE) and LVPSL were significantly improved after participants underwent RFCA. LV, left ventricle; RFCA, radiofrequency catheter ablation; bpm, beats per minute.

**Table 4** ICCs for inter and intraobserver variability for myocardial work parameters and GLS

Variable	Interobserver variability			Intraobserver variability		
	ICC	95% CI	SEM	ICC	95% CI	SEM
GWI	0.964	0.873–0.990	148.5	0.967	0.885–0.991	153.6
GCW	0.944	0.806–0.985	145.9	0.952	0.833–0.987	146.0
GWW	0.947	0.824–0.985	25.3	0.969	0.892–0.992	26.4
GWE	0.948	0.827–0.985	1.0	0.954	0.845–0.987	1.0
GLS	0.918	0.733–0.977	0.9	0.954	0.846–0.987	0.9

ICC, interclass correlation coefficient; CI, confidence interval; SEM, standard error of measurement; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency.



### Clinical implications

According to the current guidelines (1), whether asymptomatic patients diagnosed as ventricular pre-excitation should undergo RFCA (IIb, C) remains controversial, and it is not yet clear whether impaired exercise tolerance should be considered an indication for RFCA. We propose that RFCA may be considered in “asymptomatic” patients with ventricular pre-excitation free of tachycardia to impede the potential development of LV dysfunction unless contraindications are confirmed.

### Limitations

This study used a single-center design, and further investigations across multiple centers are required. Moreover, cardiopulmonary exercise tests and follow-up were not used in this study to identify the changes in exercise tolerance of the patients before and after RFCA.

### Conclusions

RFCA can improve GWW and GWE in patients with ventricular pre-excitation. In clinical practice, a noninvasive myocardial work assessment can be used in patients with ventricular pre-excitation.

### Acknowledgments

We deeply appreciate Yong Xie, Yuyang Chen, Jiajie Li, and Zeng Qu for their skillful assistance in conducting RFCA.  
*Funding:* None.

### Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist (available at <https://qims.amegroups.com/article/view/10.21037/qims-22-925/rc>).

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://qims.amegroups.com/article/view/10.21037/qims-22-925/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was

conducted in accordance with the Declaration of Helsinki (as revised in 2013), and it was approved by the Institution Review Board of Sun Yat-Sen Memorial Hospital. Written informed consent was obtained from all participants.

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**Cite this article as:** Zheng S, Zheng Y, Fang C, Xie S, Huang B, Wen K, Geng D, Zhou S. Radiofrequency catheter ablation for improving myocardial work in patients with ventricular pre-excitation. *Quant Imaging Med Surg* 2023;13(4):2660-2674. doi: 10.21037/qims-22-925

**Table S1** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation at resting HR pre- and post-RFCA

Items	Pre-RFCA				Post-RFCA			
	Left free-wall (n=18)	Septum (n=7) <sup>a</sup>	Right free-wall (n=7) <sup>a</sup>	P	Left free-wall (n=18)	Septum (n=7) <sup>a</sup>	Right free-wall (n=7) <sup>a</sup>	P
Delta, ms	48.0±9.5	43.7±6.3	48.1±9.2	0.52	–	–	–	–
QRSd, ms	128.8±16.3	128.4±16.6	135.6±10.5	0.58	81.6±10.5	87.1±10.1	80.6±8.6	0.39
PSD, ms	54.1±28.8	63.8±26.0	41.7±10.6	0.28	44.7±10.3	50.3±15.0	45.6±20.3	0.66
LVEF, %	61.8±7.5	57.9±10.5	58.4±3.9	0.41	62.2±6.0	59.9±8.9	60.7±5.1	0.69
GLS, %	–19.3±2.9	–18.7±1.9	–16.8±1.6	0.10	–19.4±2.3	–18.7±2.6	–18.0±1.3	0.36
GWI, mmHg%	1837.4±359.4	1760.6±280.8	1668.3±342.9	0.53	1843.3±235.0	1767.7±421.7	1638.4±231.3	0.28
GCW, mmHg%	2045.2±307.8	2056.3±380.5	1960.9±295.9	0.81	2084.8±237.0	2047.7±429.0	1844.7±215.7	0.17
GWW, mmHg%	148.5±55.3	215.7±100.6	158.3±42.7	0.08	93.7±38.4	111.9±60.8	70.3±21.1	0.18
GWE, %	92.6±2.4	88.1±5.9*	91.9±2.3	0.02	95.1±1.5	93.9±2.0	95.4±1.1	0.14
HR, bpm	76.3±10.3	70.4±12.7	70.3±9.3	0.30	74.8±12.6	74.6±14.9	71.4±11.5	0.83
SBP, mmHg	119.4±11.2	129.6±14.7	118.0±15.7	0.17	117.1±9.1	124.4±13.3	113.9±12.0	0.17
DBP, mmHg	73.3±7.9	75.7±6.1	75.4±7.1	0.82	72.8±6.4	73.1±4.5	74.0±8.6	0.91
Age, years old	39.3±14.3	50.1±22.8	36.1±14.2	0.24	39.3±14.3	50.1±22.8	36.1±14.2	0.24
Percentage of female (%)	33.3	57.1	42.9	0.54	–	–	–	–
Height, cm	164.7±10.0	159.3±12.5	166.6±7.1	0.36	164.7±10.0	159.3±12.5	166.6±7.1	0.36
Weight, kg	59.3±10.1	58.7±9.3	61.1±9.3	0.88	59.3±10.1	58.7±9.3	61.1±9.3	0.88

Data are expressed as mean ± standard deviation (SD). <sup>a</sup>, 1 patient was identified as intermittent ventricular pre-excitation. \* P<0.01, significantly different compared with left free-wall AVAP group. QRSd, QRS wave duration; PSD, the standard deviation of the time to the peak systolic strain of 17 segments; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.

**Table S2** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation at HR of 100 bpm pre- and post-RFCA

Items	Pre-RFCA				Post-RFCA			
	Left free-wall (n=14) <sup>a</sup>	Septum (n=7) <sup>b</sup>	Right free-wall (n=7) <sup>b</sup>	P	Left free-wall (n=14) <sup>a</sup>	Septum (n=7) <sup>b</sup>	Right free-wall (n=7) <sup>b</sup>	P
Delta, ms	51.7±10.5	49.7±8.6	49.3±10.7	0.84	–	–	–	–
QRSd, ms	135.7±26.2	138.9±19.0	136.1±10.4	0.95	80.8±10.2	85.4±14.3	83.6±6.7	0.62
PSD, ms	60.3±20.5	64.9±25.6	39.0±5.7	0.03*	52.8±14.4	54.4±14.6	41.8±6.3	0.14
LVEF, %	55.9±7.6	50.1±7.1	54.0±5.8	0.22	57.3±5.3	51.3±4.9	56.3±6.8	0.08
GLS, %	–17.1±2.3	–15.8±2.6	–15.7±2.6	0.34	–17.5±2.3	–16.2±1.9	–15.1±1.5	0.05
GWI, mmHg%	1947.1±502.0	1710.6±419.3	1676.9±361.0	0.34	1930.4±473.1	1878.3±342.5	1603.6±238.5	0.21
GCW, mmHg%	2296.0±438.2	2213.0±487.5	2010.0±488.4	0.42	2259.0±396.8	2293.0±287.7	1888.7±355.4	0.07
GWW, mmHg%	302.4±127.6	285.9±133.0	214.3±83.8	0.29	213.0±121.5	190.4±61.9	135.1±30.0	0.22
GWE, %	86.6±5.8	85.1±5.5	89.4±3.0	0.30	90.4±4.1	90.9±3.1	92.3±1.1	0.47
SBP, mmHg	139.5±15.0	145.7±16.5	130.9±29.7	0.38	137.3±12.5	146.7±16.5	132.1±27.6	0.32
DBP, mmHg	88.9±10.1	90.0±13.8	84.7±22.6	0.77	89.4±11.4	88.9±13.0	86.4±24.9	0.92
Age, years old	41.4±14.5	45.9±22.8	37.3±13.2	0.63	41.4±14.5	45.9±22.8	37.3±13.2	0.63
Percentage of female (%)	28.6	57.1	42.9	0.43	–	–	–	–
Height, cm	163.97±9.3	160.6±11.8	165.6±5.9	0.59	163.97±9.3	160.6±11.8	165.6±5.9	0.59
Weight, kg	59.9±10.0	59.9±7.4	61.9±9.8	0.89	59.9±10.0	59.9±7.4	61.9±9.8	0.89

Data are expressed as mean ± SD. <sup>a</sup>, 4 patients experienced delta wave disappearance or Wenckebach's phenomenon at pacing heart rates; <sup>b</sup>, 1 patient experienced delta wave disappearance or Wenckebach's phenomenon at pacing heart rates. \*P<0.05. QRSd, QRS wave duration; PSD, the standard deviation of the time to the peak systolic strain of 17 segments; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.

**Table S3** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation at HR of 120 bpm pre- and post-RFCA

Items	Pre-RFCA				Post-RFCA			
	Left free-wall (n=14) <sup>a</sup>	Septum (n=7) <sup>b</sup>	Right free-wall (n=7) <sup>b</sup>	P	Left free-wall (n=14) <sup>a</sup>	Septum (n=7) <sup>b</sup>	Right free-wall (n=7) <sup>b</sup>	P
Delta, ms	54.0±11.8	55.1±9.3	50.9±7.4	0.71	–	–	–	–
QRSd, ms	143.9±26.9	143.7±19.7	142.1±21.0	0.98	80.4±10.6	83.7±15.4	81.4±8.5	0.82
PSD, ms	57.4±19.7	61.2±21.9	62.9±13.8	0.80	44.2±12.7	56.6±17.6	46.7±14.2	0.19
LVEF, %	54.7±6.5	48.0±6.4	48.3±7.0	0.04*	54.9±8.3	51.0±7.2	52.6±3.1	0.48
GLS, %	–16.0±2.2	–14.8±2.4	–13.2±2.4	0.04*	–17.0±2.2	–15.4±1.9	–14.3±1.9	0.02*
GWI, mmHg%	1720.8±490.3	1422.9±437.1	1329.9±398.7	0.14	1738.4±481.8	1484.9±325.1	1204.3±311.5	0.03*
GCW, mmHg%	2170.1±295.6	2171.9±435.9	1938.3±495.1	0.40	2160.3±379.5	2066.4±312.6	1802.3±488.1	0.15
GWW, mmHg%	332.1±121.3	369.0±153.2	261.7±98.0	0.27	181.0±80.9	199.4±89.4	162.4±43.2	0.66
GWE, %	84.6±4.5	83.7±6.7	87.3±4.2	0.38	91.0±3.1	88.9±5.7	90.4±2.4	0.47
SBP, mmHg	138.3±13.3	143.4±16.5	132.6±28.4	0.56	136.2±12.5	144.1±15.1	130.1±27.7	0.35
DBP, mmHg	91.2±11.0	93.6±19.6	90.9±25.8	0.94	91.6±10.3	90.7±14.0	91.3±26.0	0.99
Age, years old	41.4±14.5	45.9±22.8	37.3±13.2	0.63	41.4±14.5	45.9±22.8	37.3±13.2	0.63
Percentage of female (%)	28.6	57.1	42.9	0.43	–	–	–	–
Height, cm	163.97±9.3	160.6±11.8	165.6±5.9	0.59	163.97±9.3	160.6±11.8	165.6±5.9	0.59
Weight, kg	59.9±10.0	59.9±7.4	61.9±9.8	0.89	59.9±10.0	59.9±7.4	61.9±9.8	0.89

Data are expressed as mean ± SD. <sup>a</sup>, 4 patients experienced delta wave disappearance or Wenckebach's phenomenon at pacing heart rates; <sup>b</sup>, 1 patient experienced delta wave disappearance or Wenckebach's phenomenon at pacing heart rates. \*P<0.05. QRSd, QRS wave duration; PSD, the standard deviation of the time to the peak systolic strain of 17 segments; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.



**Table S4** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation at resting HR

Items	Asymptomatic (n=5) <sup>a</sup>				Symptomatic (n=27)				P <sub>δ1 vs. δ2</sub>
	Pre-RFCA	Post-RFCA	δ1	P	Pre-RFCA	Post-RFCA	δ2	P	
QRSd, ms	140.4±11.8	78.0±5.7	-62.4±14.2	0.001*	128.3±15.1	83.4±10.5	-44.9±16.6	<0.001*	0.03*
PSD, ms	61.9±53.0	40.6±4.3	-21.4±54.3	0.42	52.0±18.5	47.1±14.6	-4.8±20.1	0.22	0.22
LVEF, %	54.8±5.0	59.4±6.5	4.6±8.1	0.27	61.2±7.7	61.7±6.4	0.6±4.6	0.53	0.12
GLS, %	-17.7±1.5	-18.8±2.1	-1.0±2.9	0.48	-18.8±2.7	-18.9±2.3	-0.2±1.9	0.61	0.40
GWI, mmHg%	1725.8±332.0	1901.4±245.8	175.6±292.5	0.25	1794.3±343.2	1759.9±291.8	-34.4±193.2	0.36	0.04*
GCW, mmHg%	1957.4±173.3	2154.6±185.7	197.2±313.5	0.23	2042.5±333.8	2000.0±303.5	-42.5±197.8	0.27	0.03*
GWW, mmHg%	169.0±22.7	113.6±30.0	-55.4±35.5	0.02*	164.7±74.6	88.7±43.8	-76.0±53.2	<0.001*	0.41
GWE, %	90.8±1.3	94.4±1.1	3.6±2.3	0.02*	91.6±4.1	95.0±1.7	3.4±3.1	<0.001*	0.87
HR, bpm	77.4±12.0	76.8±14.5	-0.6±4.2	0.76	73.0±10.6	73.5±12.4	0.48±8.6	0.77	0.78
SBP, mmHg	121.4±8.0	122.2±10.5	0.8±4.9	0.73	121.3±14.2	117.2±11.1	-4.1±5.6	0.001*	0.07
DBP, mmHg	71.4±7.5	72.8±5.8	1.4±2.6	0.29	74.8±10.4	73.2±6.6	-1.6±7.1	0.24	0.36
Age, years old	37.0±14.4	37.0±14.4	-	-	41.7±17.2	41.7±17.2	-	-	0.56 <sup>#</sup>
Percentage of female (%)	20	20	-	-	48.1	48.1	-	-	0.27 <sup>#</sup>
Height, cm	170.7±9.1	170.7±9.1	-	-	162.7±9.9	162.7±9.9	-	-	0.10 <sup>#</sup>
Weight, kg	57.8±6.0	57.8±6.0	-	-	59.9±10.1	59.9±10.1	-	-	0.65 <sup>#</sup>

Data are expressed as mean ± SD. δ1 and δ2 are the differences between post-RFCA values and pre-RFCA values in asymptomatic and symptomatic patients, respectively; <sup>a</sup>, 2 patients were identified as intermittent ventricular pre-excitation. <sup>#</sup>, Comparison of parameters in asymptomatic and symptomatic patients pre-RFCA. \*P<0.05. QRSd, QRS wave duration; PSD, the standard deviation of the time to the peak systolic strain of 17 segments; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.

**Table S5** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation at HR of 100 bpm

Items	Asymptomatic (n=6) <sup>a</sup>				Symptomatic (n=22) <sup>b</sup>				P <sub>δ1 vs. δ2</sub>
	Pre-RFCA	Post-RFCA	δ1	P	Pre-RFCA	Post-RFCA	δ2	P	
QRSd, ms	149.3±27.9	76.3±9.8	-73.0±29.2	0.002*	133.1±17.8	84.4±10.2	-48.8±19.2	<0.001*	0.02*
PSD, ms	70.4±26.5	52.9±20.2	-17.5±24.2	0.13	52.2±18.7	49.8±11.6	-2.4±14.4	0.43	0.06
LVEF, %	55.0±8.4	57.0±3.7	2.0±6.2	0.46	53.7±7.1	55.1±6.4	1.4±3.4	0.06	0.75
GLS, %	-16.2±2.4	-16.7±1.6	-0.5±2.2	0.60	-16.5±2.5	-16.6±2.4	-0.1±1.9	0.87	0.64
GWI, mmHg%	1732.3±291.4	1777.7±367.3	45.3±253.4	0.68	1844.5±492.0	1851.5±423.7	7.0±347.9	0.92	0.80
GCW, mmHg%	2238.3±323.4	2172.2±297.8	-66.2±381.7	0.68	2194.3±497.8	2175.7±415.6	-18.6±307.5	0.77	0.75
GWW, mmHg%	372.2±144.4	241.0±151.9	-131.2±139.9	0.07	250.1±102.9	173.4±73.0	-76.7±67.2	<0.001*	0.18
GWE, %	82.8±6.6	89.3±4.7	6.5±4.1	0.01*	88.1±4.3	91.4±2.9	3.3±3.1	<0.001*	0.05
SBP, mmHg	134.2±8.2	135.2±13.7	1.0±6.3	0.71	140.2±21.9	139.2±19.5	-1.0±6.3	0.48	0.50
DBP, mmHg	83.7±7.8	85.0±11.9	1.3±6.7	0.64	89.4±15.7	89.5±16.4	0.1±6.6	0.92	0.69
Age, years old	36.3±13.0	36.3±13.0	-	-	42.9±17.1	42.9±17.1	-	-	0.39 <sup>#</sup>
Percentage of female (%)	16.7	16.7	-	-	45.5	45.5	-	-	0.20 <sup>#</sup>
Height, cm	168.7±9.4	168.7±9.4	-	-	162.1±8.8	162.1±8.8	-	-	0.12 <sup>#</sup>
Weight, kg	56.8±5.9	56.8±5.9	-	-	61.4±9.6	61.4±9.6	-	-	0.28 <sup>#</sup>

Data are expressed as mean ± SD. δ1 and δ2 are the differences between post-RFCA values and pre-RFCA values in asymptomatic and symptomatic patients, respectively; <sup>a</sup>, 1 patient experienced delta wave disappearance at pacing heart rates.; <sup>b</sup>, 5 patients experienced delta wave disappearance or Wenckebach's phenomenon during pacing heart rates. <sup>#</sup>, Comparison of parameters in asymptomatic and symptomatic patients pre-RFCA. \*P<0.05. QRSd, QRS wave duration; PSD, The standard deviation of the time to the peak systolic strain of 17 segments; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.

**Table S6** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation at HR of 120 bpm

Items	Asymptomatic (n=6) <sup>a</sup>				Symptomatic (n=22) <sup>b</sup>				P <sub>δ1 vs. δ2</sub>
	Pre-RFCA	Post-RFCA	δ1	P	Pre-RFCA	Post-RFCA	δ2	P	
QRSd, ms	158.0±25.7	73.3±11.1	-84.7±25.5	<0.001*	139.4±21.2	83.7±10.3	-55.7±21.6	<0.001*	0.009*
PSD, ms	61.5±22.2	43.9±16.9	-17.6±25.7	0.15	59.2±17.9	49.0±14.4	-10.2±20.8	0.03*	0.46
LVEF, %	53.0±7.6	50.2±10.1	-2.8±7.5	0.39	51.0±7.2	54.2±5.9	3.2±4.9	0.006*	0.02*
GLS, %	-15.9±1.6	-16.0±1.9	-0.1±2.3	0.92	-14.7±2.7	-15.9±2.5	-1.2±2.9	0.01*	0.26
GWI, mmHg%	1758.3±342.4	1538.8±377.1	-219.5±182.3	0.03*	1491.4±495.9	1542.2±482.3	50.9±305.8	0.44	0.05
GCW, mmHg%	2259.8±186.0	1975.3±181.0	-284.5±210.7	0.02*	2072.4±419.3	2067.0±439.8	-5.5±308.6	0.93	0.04*
GWW, mmHg%	373.7±157.1	174.2±97.7	-199.5±150.2	0.02*	310.1±117.5	182.8±69.4	-127.3±80.9	<0.001*	0.12
GWE, %	84.3±5.7	90.7±4.1	6.3±5.2	0.03*	85.2±5.0	90.2±3.7	5.0±3.5	<0.001*	0.46
SBP, mmHg	136.2±12.4	131.0±12.6	-5.2±5.2	0.06	138.7±20.0	138.2±19.2	-0.5±8.4	0.80	0.20
DBP, mmHg	89.0±10.9	87.0±12.6	-2.0±4.0	0.27	92.5±18.6	92.5±16.5	0.1±5.9	0.97	0.43
Age, years old	36.3±13.0	36.3±13.0	-	-	42.9±17.1	42.9±17.1	-	-	0.39 <sup>#</sup>
Percentage of female (%)	16.7	16.7	-	-	45.5	45.5	-	-	0.20 <sup>#</sup>
Height, cm	168.7±9.4	168.7±9.4	-	-	162.1±8.8	162.1±8.8	-	-	0.12 <sup>#</sup>
Weight, kg	56.8±5.9	56.8±5.9	-	-	61.4±9.6	61.4±9.6	-	-	0.28 <sup>#</sup>

Data are expressed as mean ± SD. δ1 and δ2 are the differences between post-RFCA values and pre-RFCA values in asymptomatic and symptomatic patients, respectively; <sup>a</sup>, 1 patient experienced delta wave disappearance at pacing heart rates.; <sup>b</sup>, 5 patients experienced delta wave disappearance or Wenckebach's phenomenon during pacing heart rates. <sup>#</sup>, Comparison of parameters in asymptomatic and symptomatic patients pre-RFCA. \*P<0.05. QRSd, QRS wave duration; PSD, the standard deviation of the time to the peak systolic strain of 17 segments; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.

**Table S7** Electrocardiographic and echocardiographic parameters in patients with ventricular pre-excitation and healthy control at resting heart rate

Items	Pre-RFCA (n=32) <sup>#</sup>	Post-RFCA (n=32) <sup>#</sup>	Control (n=18)	P <sup>a</sup>	P <sup>b</sup>	P <sup>c</sup>
QRSd, ms	130.2±15.1	82.6±10.0	84.3±11.0	<0.001*	<0.001*	0.63
PSD, ms	53.5±25.8	46.1±13.6	48.6±10.2	0.11	0.37	0.66
LVEF, %	60.2±7.6	61.4±6.4	62.1±5.2	0.48	0.34	0.73
GLS, %	-18.6±2.6	-18.9±2.3	-19.4±1.7	0.57	0.22	0.44
GWI, mmHg%	1783.6±337.1	1782.0±286.2	1838.4±324.1	0.98	0.55	0.54
GCW, mmHg%	2029.2±313.5	2024.2±291.5	2128.3±330.9	0.94	0.27	0.25
GWW, mmHg%	165.3±68.8	92.6±42.5	94.8±33.4	<0.001*	<0.001*	0.88
GWE, %	91.5±3.8	94.9±1.6	94.8±1.6	<0.001*	<0.001*	0.90
HR, bpm	73.7±10.7	74.0±12.5	73.2±9.7	0.91	0.86	0.79
SBP, mmHg	121.3±13.3	118.0±11.0	118.5±11.6	0.27	0.42	0.88
DBP, mmHg	74.3±9.9	73.1±6.4	74.4±8.7	0.58	0.94	0.59
Age, years old	41.0±16.7	41.0±16.7	42.5±15.5	-	0.75	0.75
Percentage of female (%)	40.6	40.6	50.0	-	0.76	0.76
Height, cm	163.9±10.1	163.9±10.1	162.9±8.8	-	0.73	0.73
Weight, kg	59.6±9.5	59.6±9.5	62.3±8.5	-	0.31	0.31

Data are expressed as mean ± SD. <sup>a</sup>, pre-RFCA vs post-RFCA; <sup>b</sup>, Control vs pre-RFCA; <sup>c</sup>, Control vs post-RFCA. <sup>#</sup>, 2 patients were identified as intermittent ventricular pre-excitation. \*P<0.05. QRSd, QRS wave duration; PSD, the standard deviation of the time to the peak systolic strain of 17 segments; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain; GWI, global work index; GCW, global constructive work; GWW, global waste work; GWE, global work efficiency; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; RFCA, radiofrequency catheter ablation.

**Table S8** Comparison of the difference on the amount of change in GWW according to HR increase in the ventricular pre-excitation patients ( $\bar{x}\pm$ SD, n=26)

	Resting HR (73±9 bpm)	HR=100 bpm	HR=120 bpm	δ1	δ2	P <sup>a</sup>
Pre-RFCA (mmHg%)	166.7±74.2	279.6±121.9	330.6±127.6	101.5±114.9	47.9±59.1	0.05
Post-RFCA (mmHg%)	90.4±45.9	190.4±99.0	186.5±74.0	100.1±90.3	-4.0±65.7	0.001*
P <sup>b</sup>	-	-	-	0.94	<0.001*	-

δ1 = GWW<sub>100 bpm</sub> - GWW<sub>resting HR</sub>; δ2 = GWW<sub>120 bpm</sub> - GWW<sub>100 bpm</sub>; <sup>a</sup>, δ1 vs. δ2; <sup>b</sup>, pre-RFCA vs. post-RFCA. \*P<0.05. GWW, global waste work; HR, heart rate; RFCA, radiofrequency catheter ablation.

**Table S9** Comparison of the difference on the amount of change in GWE according to HR increase in the ventricular pre-excitation patients. ( $\bar{x}\pm$ SD, n=26)

	Resting HR (73±9 bpm)	HR=100 bpm	HR=120 bpm	δ1	δ2	P <sup>a</sup>
Pre-RFCA (%)	91.5±4.1	86.9±5.4	84.7±5.1	-4.7±4.7	-2.2±3.0	0.05
Post-RFCA (%)	95.0±1.7	90.9±3.4	90.2±3.8	-4.2±3.2	-0.7±3.1	0.004*
P <sup>b</sup>	-	-	-	0.44	0.11	-

δ1 = GWE<sub>100 bpm</sub> - GWE<sub>resting HR</sub>; δ2 = GWE<sub>120 bpm</sub> - GWE<sub>100 bpm</sub>; <sup>a</sup>, δ1 vs. δ2; <sup>b</sup>, pre-RFCA vs. post-RFCA. \*P<0.05. GWE, global work efficiency; HR, heart rate; RFCA, radiofrequency catheter ablation.