Insight of Electrocardiographic and Electrophysiological Parameters on The Left Ventricular Function in Patients with Ventricular Arrhythmia from Left Ventricular Summit

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Abstract

Introduction: Ventricular arrhythmia (VA) from the left ventricular summit (LVS) is a common origin of VA, which resulting LV dysfunction in some patients. However, the predictors of LV cardiomyopathy were not well-elucidated. The present study sought to investigate the risk factor of LV cardiomyopathy and the outcome in patients with LVS VA **Methods:** Between 2013 and 2018, a total of 139 patients (60.7% men; mean age 53.2 ± 13.9 years-old) underwent catheter ablation for LVS VA from two centers. Detailed patient demographics, electrocardiograms, electrophysiological characteristics, and clinical outcomes were extracted for analysis. LV cardiomyopathy was defined as LV ejection fraction (LVEF) <50%. **Results:** Acute procedural success was achieved in 92.8 % of patients. There were 40 patients (28.8%) with LV cardiomyopathy, and the mean LVEF improved from 37.5 ± 9.3% to 48.5 ± 10.2% after ablation ($p < 0.001$). After multivariate analysis, the independent predictors of LV dysfunction were wider QRS duration of the VA (odds ratio [OR]1.02; 95% confidence interval [CI]: 1.00-1.04; $p = 0.046$) and the absolute earliest activation time discrepancy (AEAD) between epicardium and endocardium (OR 1.05; 95% confidence interval CI: 1.00-1.09; $p = 0.048$). After ablation, the LV function was completely recovered in 20 patients (50%). The predictors for irreclaimable LV function included wider PVC QRS duration (OR 1.09; 95% CI: 1.02-1.17; $p = 0.012$) and poorer LVEF (OR 0.85; 95% CI: 0.74-0.97; $p = 0.020$). **Conclusion:** In patients with VA from LVS, PVC QRS duration and AEAD predicted the deteriorating LV systolic function. Catheter ablation could reverse the LV remodeling. Narrower QRS duration and better LVEF predicted a better recovery of LV function after ablation.

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Abstract

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Methods: Between 2013 and 2018, a total of 139 patients (60.7% men; mean age 53.2 ± 13.9 years-old) underwent catheter ablation for LVS VA from two centers. Detailed patient demographics, electrocardiograms, electrophysiological characteristics, and clinical outcomes were extracted for analysis. LV cardiomyopathy was defined as LV ejection fraction (LVEF) <50%.

Results: Acute procedural success was achieved in 92.8 % of patients. There were 40 patients (28.8%) with LV cardiomyopathy, and the mean LVEF improved from 37.5 ± 9.3% to 48.5 ± 10.2% after ablation ($p <$ 0.001). After multivariate analysis, the independent predictors of LV dysfunction were wider QRS duration of the VA (odds ratio [OR]1.02; 95% confidence interval [CI]: 1.00-1.04; $p = 0.046$) and the absolute earliest activation time discrepancy (AEAD) between epicardium and endocardium (OR 1.05; 95% confidence interval CI: 1.00-1.09; $p = 0.048$). After ablation, the LV function was completely recovered in 20 patients (50%). The predictors for irreclaimable LV function included wider PVC QRS duration (OR 1.09; 95% CI: 1.02-1.17; p = 0.012) and poorer LVEF (OR 0.85; 95% CI: 0.74-0.97; $p = 0.020$).

Conclusion: In patients with VA from LVS, PVC QRS duration and AEAD predicted the deteriorating LV systolic function. Catheter ablation could reverse the LV remodeling. Narrower QRS duration and better LVEF predicted a better recovery of LV function after ablation.

Keywords: Ablation; Left ventricular summit; Left ventricular function; QRS duration; Ventricular arrhythmia; absolute earliest activation time discrepancy

Introduction

Premature ventricular complex (PVC) is a common ventricular arrhythmia (VA). PVCs can cause various symptoms often regarded as benign[1, 2], but also can lead to cardiomyopathy[3, 4]. PVC-induced cardiomyopathies are characterized by deterioration of left ventricular (LV) function, which can be reversed after the elimination of PVCs [3-5]. Several parameters have been proposed to predict PVC-induced cardiomyopathy, including the PVC burden [6, 7], PVC QRS duration[8-10], origin of PVC [8], PVC coupling interval [11], symptoms, duration [12], and presence of non-sustained ventricular tachycardia (VT) or sustained VT [8]. However, except for the PVC burden, the prediction values of these parameters were inconsistent. These parameters remained debated mainly, which could be due to the heterogeneous PVC origin and the non-uniform underlying cardiac disease.

PVCs originating from epicardium have been reported as a risk factor for PVC-induced cardiomyopathy [9, 13]. The left ventricular summit (LVS) is the highest portion of the LV epicardium and is an important anatomic area harboring arrhythmogenic foci responsible for VA[14]. VAs arising from LVS frequently required multiple approach from bother epicardium and endocardial adjacent area[15]. There was no previous studies systemically investigated the incidence, risk factors, and reversibility of LV dysfunction with successful ablation.

The present study aims to determine the various factors associated with LV dysfunction induced by VA originating from LVS.

Methods

2.1 Study population

The retrospective study included 139 patients with VAs originating from the LVS who underwent electrophysiological study and three-dimensional mapping and ablation at two large centers (Taipei Veterans General Hospital and Cheng-Hsin Hospital, Taipei, Taiwan) between 2013 and 2019. The study complied with the Declaration of Helsinki, and each institutional review board approved the protocol. Data on the baseline demographic characteristics of the patient's left ventricular ejection fraction (LVEF), PVC burden, medical therapy, electrocardiographic (ECG) characteristics, use of multisite ablation, procedural details, administration of anti-arrhythmic drugs (AADs) before and after ablation, mapping parameters, and ablation outcomes were collected. The patients were divided into two groups: the patient with LV dysfunction (Group 1, LVEF less than 50%) and the patient with preserved LVEF (Group 2, LVEF [?] 50%) [16]. The routinely performed coronary angiography excluded ischemic heart disease before ablation, and significant structural heart disease was ruled out by echocardiography.

2.2 Assessment of LV function

Two-dimensional echocardiography was performed before catheter ablation and then at 3 ˜ 6 months after the procedure. Echocardiograms were performed by experienced ultrasonographers. A standard imaging protocol was used based on apical 4-chamber views according to the recommendations of the American Society of Echocardiography Two independent observers analyzed echocardiograms.[17] Three cycles were measured for each assessment, avoiding post-ectopic beats, and the average volumes were obtained.

2.3 ECG analysis of the PVC morphology and definition of the ECG criteria

With standard 12-lead ECG electrode placement, sinus rhythm (SR) and PVC ECG morphologies were measured on the BARD recording system before ablation, with the recordings displayed at 100 mm/s. PVC morphology was defined as right bundle branch block pattern (RBBB) if QRS was positive in lead V1 or left bundle branch block pattern (LBBB) for negative QRS in V1. The following measurements were also assessed manually of the first beat of PVC on the surface ECG by two independent observers: (1) coupling interval (CI); (2) QRS duration (QRSd); (3) intrinsicoid deflection time (IDT); (4) Pseudo-delta wave (PdW); (5) maximum deflection index (MDI); (6) Q-wave ratio in leads aVL and aVR[18].

CI

The CI was measured from the beginning of an SR QRS complex to the beginning of the PVC.

PVC QRSd

The PVC QRS duration (ms) was defined as the interval measured from the earliest ventricular activation to offset the QRS complex in the precordial leads.

IDT

IDT was defined as the interval measured from the earliest ventricular activation to the peak of the R wave in V2 [19].

PdW

The PdW was defined as the interval from the earliest ventricular activation to the onset of the earliest fast deflection in any precordial lead [19].

MDI

MDI was defined as the interval measured from the earliest ventricular activation to the peak of the largest amplitude deflection in each precordial lead (taking the lead with the shortest time) divided by the QRSd [20].

Electrophysiology study, mapping, and ablation

The details of the procedure protocol have been described in our previous study [21]. All VAs originated from the LVS by the definition that the earliest activation site within the LVS (great cardiac vein/anterior interventricular vein [GCV/AIV] or epicardium) based on fluoroscopy and electroanatomic mapping. The absolute earliest activation time discrepancy (AEAD) was defined as the absolute value of the difference in the earliest activation times (EAT) preceding the VA which was obtained from the epicardial (epicardium or GCV/AIV) and endocardial LVS (AEAD [ms] =—EAT_{epi}-EAT_{endo}—) [22]. Example cases of VAs from LVS with the AEAD measurement was shown in**Figure 1** .

For sustained VTs, acute procedural success was defined as noninducibility of clinical sustained VT after ablation. For patients who underwent nonsustained VT/PVC ablation, acute procedural success was defined as complete elimination, and noninducibility of frequent PVCs previously observed during the procedure [21].

Follow up

The absence of VA recurrences was assessed by 24-hour Holter monitoring and surface ECG during follow-up. VT recurrences were defined by the presence of sustained VTs, nonsustained VTs using 24- hour Holter monitoring and surface ECG and PVCs > 1000/day assessed by 24-hour Holter monitoring [21]. In addition, the assessment of the LVEF by echocardiography was repeated 3 to 6 months after ablation. LV systolic function recovery after ablation was defined as LVEF < 50% before ablation and normalization of LVEF or LVEF improved at least 15% after ablation[12, 23].

Statistical analysis

Data are expressed as the mean +- standard deviation for normally distributed continuous variables and proportions for categorical variables. The continuous variables were analyzed using a two-tailed t test. Discrete variables were compared using a $\chi 2$ test or Fisher's exact test The association between the selected parameters and PVC-induced cardiomyopathy was studied by a univariate logistic regression analysis. The variables selected for testing in the multivariate analysis for a logistic regression model were those with a P value < 0.05 in the univariate models. The differences in the LVEF before and after the ablation were compared by Student's t test. The worst LVEF before ablation was compared to those after ablation. All statistical significances were set at a P value < 0.05, and all statistical analyses were carried out using SPSS 22.0 software (IBM Corporation, Armonk, NY).

Results

Study population

As in **Table 1** , a total of 139 patients with drug-refractory PVC referred to our institute for ablation were analyzed (40 in group 1 and 99 in group 2). The characteristics of the PVCs during the 24-hour Holter monitoring were documented, with the mean PVC burden over 24 hour was 20.6 ± 11.6%, and 18.0% of patients with sustained VT and 30.2% of those with non-sustained VT. The mean LVEF was 52.4 ± 11.2%. LV dysfunction (LVEF<50%), defined by echocardiography before the ablation, was identified in 40 patients (28.8%). The origin of the PVC was confirmed to be in the LV summit, with the earliest site in the epicardium and/or GCV/AIV.

Baseline patient and PVC characteristics

The comparison of the clinical characteristics of patients with (group 1) and without LV dysfunction (group 2) is summarized in **Table 2** . The mean LVEF in group 1 was 37.5 ± 9.3% and 58.4 ± 4.1% in group 2. Compared to patients in group 2, there were more male (80.0% vs. 58.6%; $P = 0.019$), documented sustained VT (30.0% vs.13.1%;$P = 0.027$), RBBB pattern of the VA (53.4% vs. 33.5%; $P = 0.006$), longer CI (510.5

± 66.4 ms vs.483.7 ± 58.8 ms; $P = 0.021$), wider QRS duration (163.7 ± 28.0 ms vs. 147.2 ± 20.4 ms;$P = 0.001$), and larger AEAD (12.0 ± 9.1 vs. 16.3 ± 8.2 ms; P= 0.012). There was no significant difference in underlying disease, clinical presentation, baseline medical therapy, PVC burden, or the successful ablation site.

Characteristics associated with the development of LV dysfunction

In univariate analysis, as in **Table 3** , sex, presence of sustained VT, PVC morphology with RBBB pattern, CI, AEAD, and PVC QRS duration were associated with an increased risk of LV dysfunction. In multivariate analysis, only PVC QRS duration and AEAD were independently associated with the development of LV dysfunction.

Ablation outcome and changes in the LV function before and after the ablation

The overall acute success rate of the index ablation was 92.8%. The successful ablation site was most in the ASV (35.3%), followed by GCV/AIV (30.9%), subvalvular (20.9%), and epicardium (12.9%).

The changes in the PVC burden and the corresponding LVEF before and after ablation of the LV summit PVCs are shown in **Figure 2** . In patients with and without LV dysfunction, the PVC burden after the ablation was significantly decreased than that before the ablation. In group 2 patients, the LVEF before (58.4 ± 5.0%) and after (58.4 ± 5.0%) the ablation was similar ($P = 0.865$). In contrast, the LVEF significantly improved after ablation in the group 1 patients (post-LVEF vs. before-LVEF: 48.5 ± 10.2% vs. 37.5 ± 9.3%; $P< 0.001$).

During a mean follow-up period of 27.6 ± 18.4 months, 26 (18.7%) patients had recurrences with a mean duration of 9.1 ± 5.8 months after the index procedure. Of these 26 patients with recurrence, 22 patients (84.6%) had the same PVC morphology as the PVC morphology during the index procedures, and the other four patients (15.4%) had recurrences with different PVC morphology. Compared with group 2, there was a higher recurrence rate in patients in group 1 (group 1 vs. group 2: 32.5% vs. 13.1%; $P = 0.015$). Although there was PVC recurrence during follow-up, the PVC burden decreased significantly (4.8 ± 7.4%) compared to the PVC burden before the index procedure (17.6 ± 8.8%; $P< 0.001$), and the LVEF also improved significantly (post-LVEF vs. before-LVEF: 53.8 ± 11.8% vs. 48.2 ± 14.6%; $P = 0.037$). For group 1 patients, despite PVC recurrences, the PVC burden significantly decreased (2.2 ± 3.7% vs.14.5 ± 7.9%; $P < 0.001$) and there were significant improvements for LVEF after the index procedures (post-LVEF vs. before-LVEF:47.5 ± 13.0% vs.35.9 ± 8.7%; $P = 0.015$).

For 26 patients with PVC recurrences, 11 patients (42.3%) received repeat procedures (9 patients with the same PVC morphology and 2 patients with different morphology as the PVC morphology during the index procedures). Of these 11 patients, 2 patients were in group 1 and the other 9 patients were in group 2. For these 2 patients in group 1, both had LV function recovery after the index procedure (one patient with LVEF improved from 27% to 42%, and the other LVEF improved from 25% to 43%), and the LV function were similar after the repeat procedures (LVEF was 45% in both patients after the repeat procedures).

Determinants associated without LV function recovery after ablation

Of 40 patients with LV dysfunction (group 1), 20 patients (50.0%) did not recover LV function after ablation. As in **Supplemental Table I** , of these 20 patients without recovery, there were poorer LVEF at baseline (34.3 ± 7.3% vs.40.7 ± 10.1%; $P = 0.027$), longer PVC QRS duration (178.3 ± 23.1 ms vs.149.0 ± 24.9 ms; $P < 0.001$), and with more PVC recurrences after ablation than patients with LV function recovery (50.0% vs.15.0%; $P = 0.041$).

After multivariate analysis **(Supplement Table II)** , QRS duration of the PVC and baseline LVEF before the index procedure was independently predictive for irreclaimable LV function after ablation.

Discussion

Main findings

This is the first study to systematically evaluate the risk factors in developing LV dysfunction in patients with LV summit VA. In the present study, we found that:(1) The incidence of LV dysfunction with VA originated from LVS was 28.8%; (2) PVC QRS duration and AEAD were independent predictors of LV dysfunction; (3) After ablation, the LV systolic function could be improved in patients with LVS VA, and (4) PVC QRS duration and baseline LVEF before ablation were two predictors for patients with LV function recovery after ablation.

Prevalence and incidence of LV dysfunction in patients with LVS VA

The prevalence of PVC-induced cardiomyopathy has been reported at 7% among patients with a PVC burden of more than 10% [24]; however, it is likely underestimated [4]. Clinical studies have reported a diagnosis of PVC-induced cardiomyopathy from 9% to 30% of patients referred for ablation of PVC [6, 23, 25-27]. Nevertheless, most of the previous studies were heterogeneous on PVC origin, and Yamada et al. reported that PVC-induced cardiomyopathy in 19.2% of patients referred for ablation of PVC originated from RVOT[16]. In our study, with all 139 patients, the PVC originated from LV summit referred for ablation, LV dysfunction was recognized as 28.8%.

Prediction of LV dysfunction in patients with LVS VA

Most patients with PVC-induced cardiomyopathy have very frequent PVCs; however, the PVC burden alone does not reliably predict whether cardiomyopathy will be induced. Baman et al. demonstrated a PVC burden of 24% best predicted those with and without cardiomyopathy[6]. Reported cutoff numbers vary from 16% to 26%[6, 7, 24]; however, PVC-induced cardiomyopathy has been reported in patients with a PVC burden of only 4% [28], and normal heart function is often seen in patients with a high PVC burden. Similarly, in the present study with PVC originating from LV summit, the mean PVC burden before ablation was 20.6%, and it was not associated with PVC-induced cardiomyopathy. LV dysfunction could be found as low as 5% of PVC burden, and normal LV function could be noted in PVC burden as high as 55% in this large cohort. The result means that patients' characteristics and PVC features play more critical roles in the pathophysiology of PVC-induced cardiomyopathy than PVC burden.

Patients with more prolonged exposure to PVCs or an asymptomatic status have a higher risk of developing PVC-induced cardiomyopathy in asymptomatic status [12]. Patients without symptoms may have a higher probability of prolonged exposure to PVCs before they are disclosed. Of the 139 patients in our study population, only 2 (1.4%) presented without symptoms, and both had normal LV systolic function. Because most patients had symptoms, we could not conclude the association between asymptomatic status and PVC-induced cardiomyopathy in patients with VA originated from LVS.

PVC QRS duration, with a cut-ff level of >150ms best separated patients with and without PVC induced cardiomyopathy, reported by Yokokawa et al [9]. QRS duration was still be found to be the predisposing factor for LV dysfunction from the present study[9]. The result was in line with previous studies with PVCs originating from various locations throughout both ventricles. The proposed mechanisms included ventricular dyssynchrony, asymmetrically increased wall thickness, and work overload in the late activated regions, all contributing to further myocardium remodeling[4].

As previously mentioned, most studies focusing on PVC-induced cardiomyopathy were heterogeneous on PVC origin; however, there were some reports demonstrated that an epicardial origin was independently associated with PVC-induced cardiomyopathy [9, 13, 26].

Epicardial PVCs are shown to have longer QRS duration than other PVCs[9], maybe due to the paucity of Purkinje fibers in the epicardium. The initial part of the wavefront progresses slowly through the myocardial wall until reaching the Purkinje system at the subendocardium. This slow transmural activation is reflected as the slow onset of the QRS on the surface electrocardiogram [29]and prolonged transmural activation by measuring the AEAD [epi-endo]. To the best of our knowledge, this is the first study to demonstrate the relationship between PVC-induced cardiomyopathy and AEAD [epi-endo], a novel parameter associated with LV dysfunction in patients with LVS VA, which reflects the depth of intramural foci. The longer AEAD

[epi-endo] might reflect superficial epicardial foci, resulting in a longer activation time difference between epicardial and endocardial exit [22]. Although we enrolled all patients with VA originating from LVS, the wider QRS and larger AEAD [epi-endo] might indicate VA foci close to the epicardial surface, causing a long transmural activation time and LV dyssynchrony.

Catheter ablation of LVS VA and the induced LV dysfunction

Catheter ablation of PVCs has been reported to have an acute success rate of 80%-94%, with a complication rate of up to 5.6%[30-32]. However, the outcomes for catheter ablation of LVS VAs were diverse and the success rate was lower than the outcomes for PVC ablation originated other than LVS, ranging from 22% to 100% for acute procedural success and from 23% to 100% for freedom from VA recurrences [14, 18, 33, 34]. In the present study, ablation of LVS VAs was effective, with a high acute success rate (92.8%). Also, in patients with LV dysfunction, the decreased LVEF improved from 37.5 ± 9.3% to 48.5 ± 10.2% ($P < 0.001$), indicating the reversible phenomenon of PVC-induced cardiomyopathy, which was comparable to previous studies showing that after successful ablation of the PVCs originated from various locations, there was a mean improvement of LVEF from 10%-15% [13, 26, 31, 35, 36].

In the present study, 50% of patients recovered LV systolic function. For patients without recovery, we found that longer VA QRS duration and poorer LVEF before ablation were two independent factors in predicting irreclaimable LV dysfunction. Our study was in accordance with previous study [37]. Combining with the poor LVEF as another prediction, the results echoed our postulation that patients with longer PVC QRS duration may have more severe and irreversible underlying LV substrate abnormalities, which was an indicator rather than a cause for LV cardiomyopathy.

Clinical Implications

LVS has been demonstrated to be an essential anatomic focus for the origin of VA. According to the present study, the incidence of LV dysfunction in patients with frequent VA from LVS PVC is high (28.8%). A significant improvement in LV systolic function in patients with LVS VA-induced cardiomyopathy could be achieved after successful ablation. The discrepancy of activation (between endocardium and epicardium) and the QRSd were the only predictors for LV dysfunction; hence, patients with longer QRS duration should be advocated for an earlier intervention to eliminate the VA.

Study limitations

There were several limitations for the present study. First, the present results were obtained from relatively small study samples and retrospective in nature, besides, no control group was included in the present study. The prospective, randomized study with large sample size to validate the results is mandated. Second, we did not collect cardiac magnetic resonance (CMR) data, and therefore, myocardial fibrosis before the ablation could not be analyzed and limiting us to detect significant CMR predictors of the development of PVC induced cardiomyopathy. Third, the VA duration was proved to be a predictor for VA induced cardiomyopathy [12], and which was not collected in the present study.

Conclusion

In patients with VA originating from LVS, LV dysfunction could be reversed by catheter ablation. VA QRS duration and the AEAD were the only predictors of LV dysfunction. The VA QRS duration and the baseline LVEF could predict the reversibility of LV dysfunction after catheter ablation.

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Figure legend

Figure 1. The activation map of two patients with symptomatic premature ventricular complex originated from the left ventricle summit. Figure (A) and (B) showed one patient with premature ventricular complex (PVC) with QRS duration 142ms. Figure (B) showed the earliest activation site was localized over the distal great cardiac vein (GCV) (EAT: 29 ms pre-QRS), while in Figure (A) the earliest activation within the left ventricle (LV) was located at LV summit region over left ventricular outflow tract (LVOT), just opposite to the EAT of the distal GCV (EAT: 22 ms pre-QRS). The AEAD was 7 (=—29-22—) ms. The patient pre-procedural LV ejection fraction (LVEF) was 55%, and it was 61% after the procedure. Figure (C) and (D) showed another patient with PVC with QRS duration 174ms. Figure (D) showed the earliest activation site was originated from the distal GCV (EAT: 35 ms pre-QRS), while in Figure (D), the earliest activation site within the LV endocardium was located near LV summit region over LVOT (EAT: 20ms pre-QRS). The AEAD was 15 (=—35-20—) ms. The patient pre-procedural LVEF was 36%, and it became 43% after the ablation procedure. LV, left ventricle; RVOT, right ventricular outflow tract.

Figure 2. The changes of the PVC burden and the LVEF before and after ablation. Panel A showed the changes of the PVC burden before and after the ablation in those with or without PVC induced cardiomyopathy. Panel B showed changes of LVEF before and after ablation in those with or without PVC induced cardiomyopathy. PVC, premature ventricular complex; LVEF, left ventricular ejection fraction; CMP, cardiomyopathy. $*P < 0.001$

Figure 1.

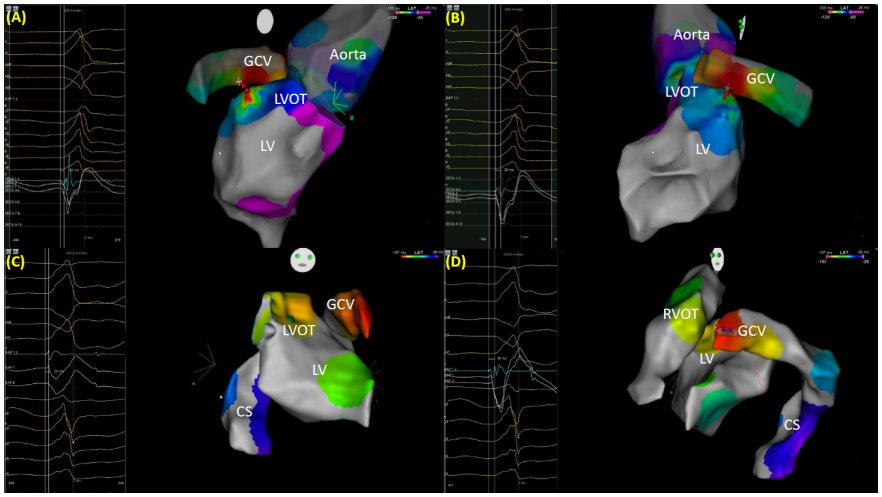

Figure 2.

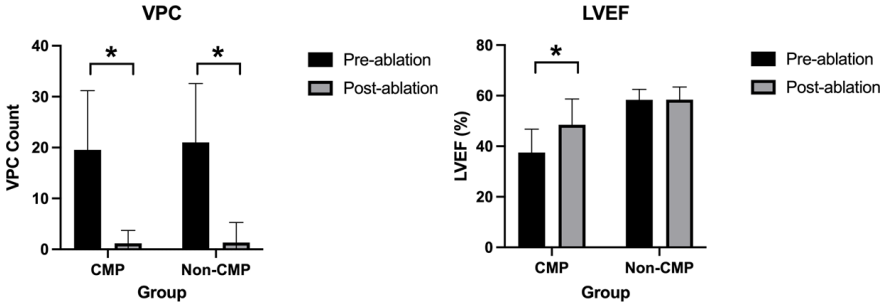

Table 1. Patient Characteristics (N = 139)

Variables
Age, years old
Male (n, %)
Hypertension (n, %)
Diabetes (n, %)
Symptom of Palpitation (n, %)
Symptom of Syncope (n, %)
Medication before ablation
Beta blocker or CCB only (n, %)
Class I AAD (n, %)
Amiodarone (n, %)
Clinical VA pattern
Presence of Sustained VT (n, %)
Presence of Non-Sustained VT (n, %)
PVC burden (pre-ablation) (beats/day)
PVC burden (pre-ablation) (%)*
LVEF (pre-ablation) (%)*
PVC induced cardiomyopathy (n, %)
VA morphology
RBBB morphology (n, %)

Coupling interval
QRSd, ms
IDT, ms
PdW, ms
Q-wave aVL/aVR ratio
MDI
Earliest activation before VA (ms)
Multiple site ablation requirement (n, %)
Successful ablation site (n, %)
ASV
Subvalvular
GCV/AIV
Epicardium
Acute procedural success (n, %)
AAD, anti-arrhythmic drug; AIV, anterior Interventricular vein; ASV, aortic sinus of Valsalva; CCB, calcium channel blocke

Table 2. Comparisons of the factors between patients with or without cardiomyopathy

	Normal LV function (N = 99)	**LV cardiomyopathy (N = 40)**	***P* value**
Age (y/o)	52.3 ± 13.5	55.3 ± 15.0	0.254
Male (n, %)	58 (58.6%)	32 (80.0%)	0.019
Hypertension (n, %)	17 (17.2%)	6 (15.0%)	1.000
Diabetes (n, %)	8 (8.1%)	3 (7.5%)	1.000
Symptom of Palpitation (n, %)	97 (98.0%)	40 (100.0%)	1.000
Symptom of Syncope (n, %)	10 (10.1%)	7 (17.5%)	0.257
Medication before ablation			
Beta blocker or CCB only (n, %)	39 (39.4%)	15 (37.5%)	1.000
Class I AAD (n, %)	36 (36.4%)	13 (32.5%)	0.700
Amiodarone (n, %)	19 (19.2%)	12 (30.0%)	0.182
Clinical VA pattern			
Presence of Sustained VT (n, %)	13 (13.1%)	12 (30.0%)	0.027
Presence of Non-Sustained VT (n, %)	33 (33.3%)	9 (22.5%)	0.228
PVC burden (pre-ablation) (beats/day)	22467 ± 12419	20597 ± 12307	0.510
PVC burden (pre-ablation) (%)*	20.9 ± 11.6	20.0 ± 11.6	0.631
Ejection fraction (pre-ablation) (%)*	58.4 ± 4.1	37.5 ± 9.3	<0.001
VA morphology			
RBBB morphology (n,%)	27 (27.3%)	19 (47.5%)	0.029

	Normal LV function (N = 99)	**LV cardiomyopathy (N = 40)**	***P* value**
Coupling interval	483.7 ± 58.8	510.5 ± 66.4	0.021
QRSd, ms	147.2 ± 20.4	163.7 ± 28.0	0.001
IDT, ms	58.2 ± 20.8	63.8 ± 21.9	0.155
PdW, ms	56.9 ± 20.7	59.9 ± 20.4	0.438
Q-wave aVL/aVR ratio	1.36 ± 0.48	1.49 ± 0.39	0.130
MDI	0.47 ± 0.13	0.46 ± 0.13	0.617
Successful ablation site (n, %)			
ASV	38 (38.4%)	11 (27.5%)	0.246
Subvalvular	21 (21.2%)	8 (20.0%)	1.000
GCV/AIV	28 (28.3%)	15 (37.5%)	0.315
Epicardium	12 (12.1%)	6 (15.0%)	0.781
AEAD	12.0 ± 9.1	16.3 ± 8.2	0.012
Multiple site ablation requirement (n, %)	56 (56.6%)	22 (55.0%)	1.000

Table 3. Multivariate analysis for predictors of cardiomyopathy in the patients with VA from LV summit.

Age								
Male								
Hypertension								
Diabetes								
Symptom of syncope								
Clinical VA pattern								
Presence of sustained VT								
Presence of NSVT								
PVC burden (pre-ablation), %*								
VA morphology*								
RBBB morphology								
Coupling interval								
QRSd, ms								
IDT, ms								
PdW, ms								
Q aVL/aVR ratio								
MDI								
Successful ablation site								
ASV								
Subvalvular								
GCV/AIV								
Epicardium								
AEAD								
Multiple site ablation requirement								

AAD, anti-arrhythmic drug; AEAD, absolute earliest activation time discrepancy; AIV, anterior Interventricular vein; ASV,

Supplemental Table 1. Comparisons of factors between LV function recovery or not in PVC induced

cardiomyopathy after RFA.

	Without recovery (N = 20)	**With recovery (N = 20)**	***P* value**
Age (y/o)	59.7 ± 14.6	50.8 ± 14.3	0.059
Male (n, %)	18 (90.0%)	14 (70.0%)	0.235
Hypertension (n, %)	3 (15.0%)	3 (15.0%)	1.000
Diabetes (n, %)	2 (10.0%)	1 (5.0%)	1.000
Medication before ablation			
Beta blocker or CCB only (n, %)	7 (35.0%)	8 (40.0%)	1.000
Class I AAD (n, %)	8 (40.0%)	5 (25.0%)	0.501
Amiodarone (n, %)	5 (25.0%)	7 (35.0%)	0.731
Presence of Sustained VT (n, %)	9 (45.0%)	3 (15.0%)	0.082
Presence of Non-Sustained VT (n, %)	5 (25.0%)	4 (20.0%)	1.000
PVC burden (pre-ablation) (beats/day)	21267 ± 10968	19760 ± 14266	0.759
PVC burden (pre-ablation) (%)*	19.5 ± 9.3	19.8 ± 14.3	0.948
Ejection fraction (pre-ablation) (%)*	34.3 ± 7.3	40.7 ± 10.1	0.027
VA morphology			
RBBB morphology (n,%)	10 (50.0%)	9 (45.0%)	1.000
Coupling interval	522.0 ± 75.6	499.0 ± 55.3	0.278
QRSd, ms	178.3 ± 23.1	149.0 ± 24.9	<0.001
IDT, ms	64.7 ± 24.3	63.0 ± 19.9	0.815
PdW, ms	57.4 ± 20.5	62.5 ± 20.5	0.432
Q-wave aVL/aVR ratio	1.55 ± 0.43	1.44 ± 0.36	0.376
MDI	0.44 ± 0.13	0.48 ± 0.12	0.271
Earliest activation before VA (ms)	-41.2 ± 10.2	-40.5 ± 24.2	0.906
Successful ablation site (n, %)			
ASV	5 (25.0%)	6 (30.0%)	1.000
Subvalvular	6 (30.0%)	2 (10.0%)	0.235
GCV/AIV	7 (35.0%)	8 (40.0%)	1.000
Epicardium	2 (10.0%)	4 (20.0%)	0.661
Multiple site ablation requirement (n, %)	14 (70.0%)	8 (40.0%)	0.111
AEAD	16.3±8.6	16.3±7.9	0.985
Acute procedural success (n, %)	18 (90.0%)	17 (85.0%)	1.000
PVC recurrence (n, %)	10 (50.0%)	3 (15.0%)	0.041

AAD, anti-arrhythmic drug; AEAD, absolute earliest activation time discrepancy; AIV, anterior Interventricular vein; ASV, aortic sinus of Valsalva; CCB, calcium channel blocker; GCV, great cardiac vein; IDT, intrinsicoid deflection time; LVEF, left ventricular ejection fraction; MDI, maximum deflection index; VA, ventricular arrhythmia; PdW, pseudo-delta wave; VT, ventricular tachycardia; PVC, premature ventricular complex; QRSd, QRS duration; RBBB, right bundle branch block;

Supplemental Table 2. Multivariate Analysis for Predictors of persistent LV dysfunction after RFA.

	Univariate analysis Crude OR	Univariate analysis 95% CI	Univariate analysis P value	Multivari Adjusted
Age	1.04	0.99-1.09	0.065	1.09
Male	3.86	0.67-22.11	0.130	
Hypertension	1.00	0.18-5.67	1.000	
Diabetes	2.11	0.18-25.35	0.556	
Presence of sustained VT	4.64	1.02-21.0	0.047	14.88
Presence of NSVT	1.33	0.30-5.93	0.705	
PVC burden (pre-ablation), %*	0.99	0.93-1.07	0.943	
LVEF (pre-ablation)	0.92	0.85-0.99	0.036	0.85
VA morphology*				
RBBB morphology	1.22	0.35-4.24	0.752	
Coupling interval	1.01	0.99-1.02	0.280	
QRSd, ms	1.05	1.02-1.08	0.003	1.09
IDT, ms	1.00	0.98-1.03	0.810	
PdW, ms	0.99	0.96-1.02	0.422	
Q aVL/aVR ratio	2.13	0.41-11.06	0.368	
MDI	0.50	0.01-9.72	0.266	
EAT	0.99	0.96-1.03	0.903	
Successful ablation site	Successful ablation site	Successful ablation site	Successful ablation site	Successfu
ASV	0.78	0.19-3.13	0.724	
Subvalvular	3.86	0.67-22.11	0.130	
GCV/AIV	0.81	0.22-2.91	0.744	
Epicardium	0.44	0.07-2.76	0.384	
Multiple site ablation requirement	3.50	0.95-12.97	0.061	
AEAD	0.999	0.926-1.079	0.984	
Acute procedural success	1.59	0.24-10.70	0.635	
PVC recurrence	5.67	1.25-25.61	0.024	12.56

AAD, anti-arrhythmic drug; AEAD, absolute earliest activation time discrepancy; AIV, anterior Interventricular vein; ASV, aortic sinus of Valsalva; CCB, calcium channel blocker; GCV, great cardiac vein; IDT, intrinsicoid deflection time; LVEF, left ventricular ejection fraction; MDI, maximum deflection index; VA, ventricular arrhythmia; PdW, pseudo-delta wave; VT, ventricular tachycardia; PVC, premature ventricular complex; QRSd, QRS duration; RBBB, right bundle branch block;