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Original Article

Reversal of premature ventricular complexes induced cardiomyopathy. Influence of concomitant structural heart disease

Mohamed A. Abdelhamid*, Rania Samir

Department of Cardiovascular Medicine, Faculty of Medicine, Ain Shams University, Egypt

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ABSTRACT

Background: We examined the effect of radiofrequency (RF) catheter ablation of premature ventricular complexes (PVCs) on left ventricle (LV) function recovery in patients with LV dysfunction, regardless the presence of structural heart disease (SHD).

Methods: Seventy seven patients with impaired LV ejection fraction (EF) (37.1 ± 9.4), suspected to have PVCs cardiomyopathy (PVC-CM) (>10% PVCs burden), referred for RF ablation were enrolled, and divided into 2 groups according to the presence of SHD. SHD was ruled out by echocardiography, coronary angiography or MRI. CARTO 3 mapping system was used employing activation mapping in the majority of cases. Initial success was defined as complete elimination or residual PVCs ≤ 10 beats/30 min. Long term success was defined as reduction in PVCs burden >80% on follow-up holter. Echocardiography was done after 6 months. Improvement of EF >5% was considered significant.

Results: Forty two (55.8%) cases had SHD. PVCs burden was 28.4 ± 9.8%. EF improved to 48.6 ± 10.3. Initial success, overall success, post procedural PVCs burden and EF were comparable in both groups. EF improved in 47(75%) of successful cases with no significant differences between both groups. Post-MI Patients were the least category to improve. PVCs burden before and after ablation were the independent predictors of LVEF recovery by multivariate analysis. Cutoff values of >18%, <8% had 100% sensitivity and 85%, 87% specificity, respectively.

Conclusions: PVCs elimination by RF ablation results in significant improvement even restoration of LV function regardless of PVC origin, or the presence of concomitant SHD. PVCs burden before and after ablation are the main predictors of LVEF recovery.

1. Introduction

Premature ventricular complexes (PVCs) are early depolarization of the myocardium originating in the ventricle, often seen in association with structural heart disease (SHD). According to the current ESC 2015 guidelines, frequent PVCs in patients with SHD are associated with increased mortality rate.[1,2]

Frequent PVCs are a main cause of reversible cardiomyopathy. However, the majority of the patients presenting with frequent PVCs will not develop cardiomyopathy and the prevalence of PVCs induced cardiomyopathy (PVC-CM) does not exceed 5% to 7% in patients with a PVCs burden >10%. In addition, the accurate diagnosis of PVC-CM is difficult and should rule out other underlying causes and follow up of left ventricle (LV) function after arrhythmia control to ensure direct causal relation.[3,4]

Elimination of frequent PVCs by antiarrhythmic drugs or radiofrequency (RF) ablation may improve or restore normal LV function. Currently, catheter ablation and amiodarone are class IIa indication.[2]

The presence of underlying/concomitant SHD could add to the clinical significance and the outcome of PVCs elimination.[5] We examined the effect of RF catheter ablation of monomorphic PVCs on LV function recovery in patients with LV dysfunction, regardless the presence or absence of SHD.

2. Methods

2.1. Study population

Seventy seven patients with LV dysfunction (ejection fraction <50%), and very frequent (>10% PVCs burden documented on holter monitoring)[6] monomorphic PVCs, refractory to medical treatment, in the presence or absence of SHD, referred for RF ablation at Ain Shams University EP-lab during the period from May 2015 to August 2016, were enrolled in the current study.

* Corresponding author.
E-mail addresses: Amein1000@yahoo.com (M.A. Abdelhamid), raniasamir_3@icloud.com (R. Samir).

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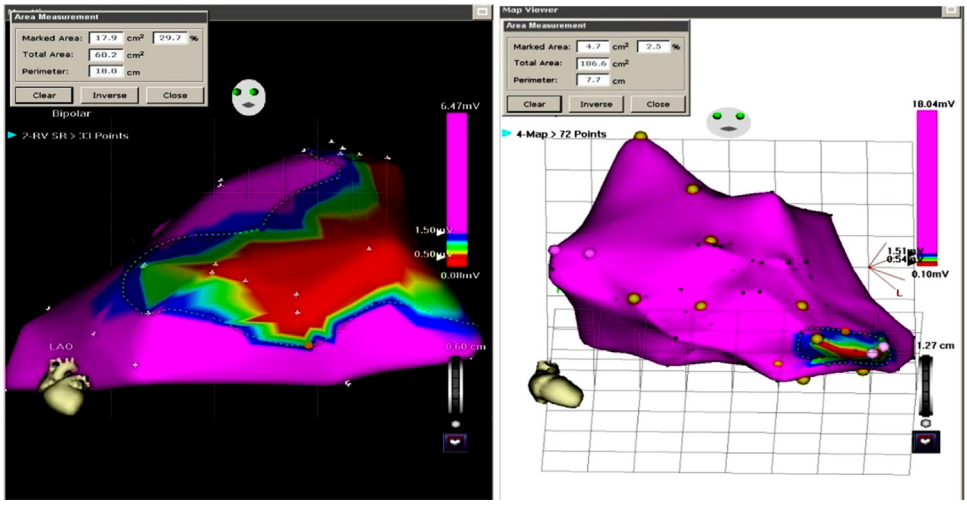

Fig. 1. Voltage maps of 2 patients with SHD. Right panel showing small apical scar in a patient with dilated cardiomyopathy and normal coronary angiogram. Left panel showing anterolateral scar in patient with old MI and revascularized with stenting.

Patients with sustained ventricular tachycardia, non revascularized coronary artery disease (CAD), concomitant atrial arrhythmias, NYHA class III or IV, and those with epicardial origin of PVCs were excluded.

2.2. Methodology

Full medical history, clinical examination and standard laboratory investigations were performed to rule out reversible PVCs etiology and to ensure patients were compliant on appropriate medical therapy.

2.3. Baseline 12 lead ECG, holter monitoring, and echocardiography

Preliminary localization of PVC origin from the resting ECG was done using common algorithms.[7] 12 lead ECG was mainly valuable in cases where pace mapping protocol was used in case of infrequent or no inducible PVCs. 24 h holter monitoring was performed before RF ablation and 6 months after. In the presence of significant symptoms, holter was done at any time during follow-up period to rule out early or late recurrence.

Coronary angiography was done to rule out significant CAD. Standard 2D echocardiographic examination was done in to identify SWM abnormalities, significant valvular disease, hypertrophic or infiltrative cardiomyopathies. In addition, cardiac MRI was used in selected cases (mainly in cases with suspected arrhythmogenic RV dysplasia).

Echocardiographic examinations were done before and 6 months after RF ablation. LV ejection fraction (LVEF) was calculated by modified Simpson method. LVEF $<50\%$ was considered abnormal. Improvement of EF $\geq 5\%$ at the end of the follow-up was considered significant for further statistical analysis.[8] All examinations were done by the same physician who was blinded to the study results to avoid inter-observer variability.

2.4. Electrophysiologic study (EP) study and RF ablation

The procedure was done under conscious sedation in the fasting state after giving a written informed consent. Antiarrhythmic drugs were stopped for at least 5 half-lives before the procedure and none of the cases was given medical treatment after successful ablation.

3D electro-anatomical mapping was done for all cases using the CARTO 3 mapping system (Biosense, Diamond Bar, CA, USA) using compatible ablation catheters (8F irrigated tip Navistar or Ezesteer), with a temperature limit of 48 °C and maximum power of 30–40 W. Activation maps were created in the majority of cases. Ablation target was the site of earliest ventricular activation with local ventricular electrogram preceding the surface QRS onset by 25–30 msec. Pace mapping protocol was used in case of infrequent PVCs targeting sites with perfect pace maps score 12/12. RF energy was delivered 60 to 120 s at each ablation site. Voltage maps were created simultaneously to identify ventricular endocardial scars. Cases with endocardial scars were classified as having SHD even in absence of identifiable etiology (Fig. 1).

Initial success was defined as complete elimination of PVCs or residual PVCs ≤ 10 beats/30 min while long term success was defined as reduction in PVCs burden $>80\%$.[9]

Patients were kept in the hospital for 24 h after procedure to rule out complications and were followed up for a mean period of 5.8 ± 1.4 months.

The study protocol was approved by the Research and Ethics Committee of the Cardiology Department, Ain Shams University.

2.5. Statistics

Data were analyzed using SPSS version 21 for Windows and graphics by MS Excel. Categorical data were expressed as frequencies and percentages, while continuous data were expressed as mean $\pm$ SD or median. Comparison between categorical variables was done using Chi square or Fisher's exact test as appropriate. Comparison between continuous variables was done using *t*-test or Mann-Whitney test according to normality of distribution. P value was considered significant if <0.05. Logistic regression analysis was used to identify predictors of echocardiographic response. Receiver operating characteristics (ROC) curve analysis was done and cutoff values were selected if area under the curve (AUC) was significantly different from 0.5. A p value <0.05 was considered statistically significant.

3. Results

Seventy seven patients with impaired LV systolic function (mean EF 37.1 ± 9.4), suspected to have PVC-CM ($>10\%$ PVC

Table 1
Baseline features of the study group.

	Group A (Idiopathic) n = 35	Group B (SHD) n = 42	p value
Age (years)	43.4 ± 12.8	44.9 ± 13.5	NS
Male gender (n)	22(62%)	23(54%)	NS
PVC origin			
RVOT	10(28.5%)	6(14%)	NS
LVOT	16(45%)	27(64%)	
others	9(25.7%)	9(21.5%)	
Symptoms			
Duration (years)	5.4 ± 2.4	6.2 ± 2.8	NS
Dyspnea (n)	28(80%)	36(85.7%)	NS
Palpitation (n)	29	31	NS
Syncope (n)	2	3	NS
Treatment			
Amidarone (n)	18	23	NS
ACEI	34	42	NS
Beta blockers (n)	33	39	NS
Spironolactone	22	18	NS
Baseline echo parameters			
LVEDD (mm)	60.2 ± 4.3	61.4 ± 6.9	NS
LVESD (mm)	46.7 ± 4.1	47.8 ± 6.0	NS
2D EF	38.1 ± 8.5	36.8 ± 7.1	NS
Baseline holter parameters			
PVC burden (%)	28.00 ± 10.05	30.76 ± 9.91	NS
PVC (n)	28057.2 ± 9067	30843.2 ± 14303.2	NS
Bigeminy cycles (n)	5250.94 ± 10608.45	4696.75 ± 6696.5	NS
Couplets (n)	835.52 ± 1926.06	1111.30 ± 3315.64	NS
NSVT (n)	87.76 ± 264.15	96.10 ± 207.41	NS

PVC: premature ventricular complexes; RVOT: right ventricular outflow tract; LVOT: left ventricular outflow tract; ACEI: angiotensin-converting-enzyme inhibitor; LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; NSVT: non sustained ventricular tachycardia; NS: non significant.

burden) were enrolled. Mean age of study group was 42.9 ± 16.1 years, including 45 (58%) males. 42(55.8%) cases had SHD diagnosed either before enrollment or by baseline workup, and classified as group B (18 had ischemic heart disease with old myocardial infarction in the majority (15) with previous stenting (7) or bypass grafting (3), 14 had known dilated cardiomyopathy, 7 had significant valvular disease with previous valve replacement in 5 cases, 2 had arrhythmogenic RV dysplasia and the remaining patient had patchy LV myocardial scarring suggesting old myocarditis.

Mean PVCs number was 29520 ± 12035, burden was 28.4 ± 9.8%. PVCs originated in outflow tract (OT) in the majority of cases (76.6%), more in left ventricular outflow tract (LVOT) (55.8%) followed by right ventricular outflow tract (RVOT) (20.7%), tricuspid or mitral annulus (9%), para-hisian (7.7%), and papillary muscle origin (6.4%) in order of frequency. Shortness of breath was the overwhelming complaint with the mean symptom duration of 5.8 ± 3.5 years (Table 1).

3.1. Procedural aspects

Initial success was achieved in 71 (92.2%) cases, while long-term success rate excluding recurrent cases was achieved in 62 (80.5%) cases, with no significant difference between both groups. However, mean procedural time, fluoroscopic time, and number of ablation trials were significantly higher in the SHD group. Six months holter parameters were comparable with no significant differences. Procedural complications occurred infrequently and included ventricular fibrillation in 3 patients related to adrenaline provocation and puncture site hematoma in 2 cases. One patient died 3 months after the procedure with worsening heart failure with no direct causal relation to the procedure (Table 2, Fig. 2).

3.2. Follow up echocardiographic findings

Mean EF improved significantly in the whole study group (48.6 ± 10.3 vs 37.1 ± 9.4). Also significant reduction was observed in LV internal dimensions: 57.6 ± 5.5 vs 60.5 ± 5.8, and 41.6 ± 6.2 vs 47.1 ± 5.6, for left ventricular end diastolic diameter (LVEDD) and end-systolic diameter (ESD), respectively, with no significant differences between both study groups. Magnitude of EF improvement was also comparable (Table 3). However, subset of patients with ischemic heart disease (n = 18) had the least degree of improvement in EF when compared to the rest of the group (n = 24) with SHD (6.8 ± 5.4% vs 12.8 ± 9.8%, $p < 0.01$).

3.3. Predictors of LVEF improvement

EF improved significantly (>5%) in 47 cases with successful ablation, representing 61% of the studied population and 75% of patients with successful ablation, without significant difference between both study groups (24(68%) in idiopathic group and 23

Table 2
Procedural aspects in the study group.

	Group A n = 35	Group B n = 42	p
Activation mapping	32(91%)	40(95%)	NS
Time of earliest activation signal preceding QRS (ms)	43.82 ± 8.55	44.65 ± 13.28	NS
Procedural time (min)	102.94 ± 30.27	133.50 ± 29.57	<0.01
Fluoroscopy time (min)	34.41 ± 11.04	41.55 ± 10.85	<0.01
Ablation Power (Watt)	35.29 ± 1.61	34.5 ± 3.007	NS
Ablation temperature (C)	51.76 ± 5.22	50.55 ± 4.43	NS
Impedance (ohms)	111.70 ± 9.42	112.80 ± 9.02	NS
Ablation time (sec)	388.82 ± 149.91	441.00 ± 214.37	NS
Ablation trials	3.52 ± 2.00	4.65 ± 2.47	<0.05
Complications/mortality (n)	3/0	2/1	NS
Initial success	33(94.2%)	38(90.4%)	NS
Long term success	29(82.8%)	33(78.5%)	NS
Follow up holter parameters			
PVB burden (%)	2.21 ± 5.82	4.8 ± 11.45	NS
PVB (n)	2207.48 ± 6540.36	5530.68 ± 18391.7	NS
Bigeminy cycles (n)	10.29 ± 40.15	108.36 ± 244.86	<0.05
Couplets (n)	445.05 ± 1924.73	786.32 ± 3439.54	NS
NSVT (n)	29.4 ± 125.6	28.6 ± 127.9	NS

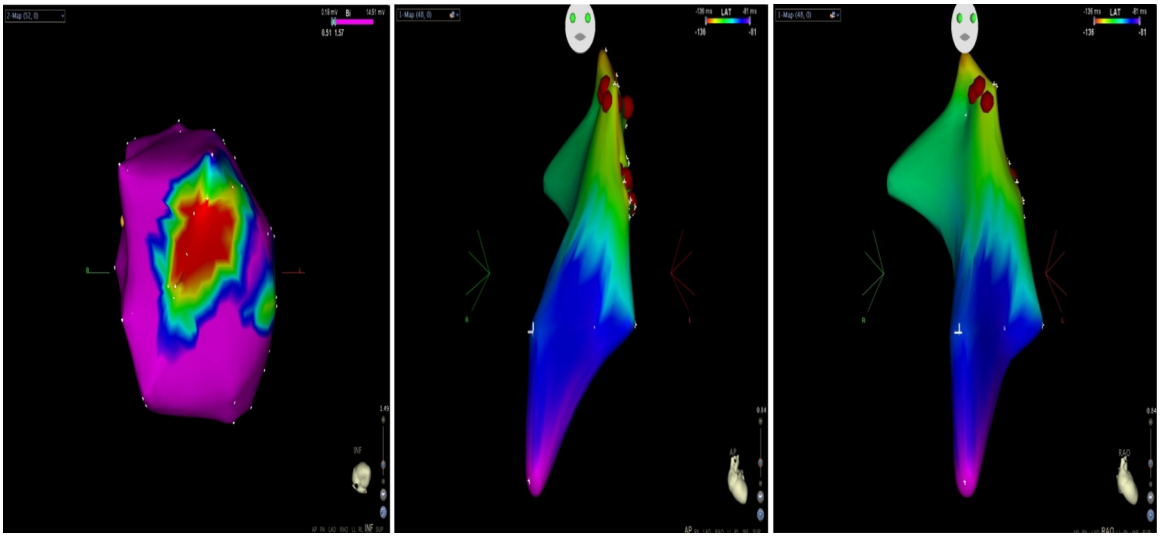

Fig. 2. Voltage map inferior view showing apical and para-apical scar (left panel), activation map showing PVC origin in RVOT septum (middle (AP) and right (RAO) panel) in a group B case.

(56%) in the SHD group, $p > 0.05$). Significant EF improvement occurred in 30 (60%) cases with LV origin compared to 17(65%) cases with RV origin, $p > 0.05$. PVCs burden before and after ablation i.e long term success appeared to be the only independent predictors of LV function recovery by multivariate analysis. Cutoff values of >18% for PVCs burden before ablation, and <8% for PVCs burden after ablation, had 100%, sensitivity and 85%, 87% specificity, respectively (Table 4, Fig. 3).

4. Discussion

PVCs are the most common arrhythmias encountered during clinical practice and the usual attitude of the cardiologists is reassurance particularly in healthy subjects. However, in patients with SHD, PVCs are not that benign and are linked to sudden cardiac death.[2] Frequent PVCs can cause LV dysfunction even in absence of concomitant SHD (PVC-CM) but the mechanisms are largely debated.[1–4] The current study included 77 patients with depressed EF (37.1 ± 9.4) and frequent (>10%) PVCs referred for RF ablation and were divided into two groups based on the absence or presence of SHD.

Mean PVCs burden in the current study was 28.4 ± 9.8% and the mean symptom duration was 5.8 ± 3.5 years. Predictors of PVC-CM were extensively studied over the past decade and included LV/RV location of the focus, coupling interval, PVC axis, polymorphism, PVC duration or amplitude, post-PVC pause duration, bigeminy/trigeminy, percent interpolation, symptom duration of 30–60 months, lack of symptoms, PVCs burden, and epicardial PVC origin.[10–12] The latter three factors were mentioned to be the independent predictors among the fore-mentioned parameters in a recent large multicenter case control study.[13] Cut off values of PVCs burden of 16%, 24%, 26% were established in different studies.

Table 3
Post ablation 6 months echocardiographic data.

	Group A n = 35	Group B n = 41	P
LVEDD(mm)	56.2 ± 4.1	57.4 ± 5.9	NS
LVESD(mm)	41.5 ± 5.1	41.8 ± 9.0	NS
EF%	49.4 ± 9.7	47.2 ± 11.8	NS
EF improvement	11.3 ± 8.5	10.4 ± 8.9	NS

However, the development of PVC-CM with lower thresholds (as low as 4%), and the low incidence of LV dysfunction in general (5–7%) with high thresholds, in addition to daily variability in PVCs burden, have led many to the conclusion that the development of PVC-CM is mainly patient dependant and that factors other than the crude PVCs number are necessary to induce cardiomyopathy.[4,13–16]

Most of available reports focused on PVCs burden as risk factor for PVC-CM. In the current study, all patients had impaired EF but PVCs burden before RF ablation was an independent predictor of LV function recovery after ablation. A cut off value of >18% had 100% sensitivity and 85% specificity. Very few studies have reported relevant data where cut off values of 13%, or >20000/24 h predicted >5% increase in LVEF after RF ablation. This finding was consistent among patients with resting normal EF or those with LV dysfunction in absence or presence of SHD like in the current study.[17,18]

Shortness of breath was the overwhelming symptom in this study, possibly due to relatively low EF. Relevant data were previously reported.[17] LV was the most common site of origin of PVCs in the current study mainly outflow tract. Nearly two-third of idiopathic PVCs originate in the outflow tract mainly RVOT due to emberyological, anatomical (transitional zone), and genetic factors.[10,19,20] In the current study, LVOT and RVOT origin were comparable (45% vs 29%) in the idiopathic group. In SHD group, LV origin was predominant, but the majority also originated in LVOT (64%) followed by other sites like annulus, and papillary muscle (21%). We did not encounter any PVCs within scar tissue and only 15% of the cases were in peri-infarct (scar) area. Relevant data were reported in a similar larger cohort of patients by *Marie Sadron* and colleagues (LV origin in the majority (68%) of cases, LVOT origin was the commonest site (28%) followed by epicardial and RVOT locations (24% and 21%, respectively), and PVCs were not related to site of mycardial infarction (scar).[13] Others have reported even more frequent (78%) origin from LV in cases with SHD, but the site of origin within LV was almost distributed between LVOT, scar related, followed by epicardial locations.[17] The inclusion of patients with sustained ventricular tachycardia and >1 PVC morphology in the latter study, together with the exclusion of patients with epicardial foci in the current study, may explain these differences and raised the percentage of LVOT cases.

Table 4
Predictors of LVEF recovery by univariate and multivariate analysis.

	Univariate		Multivariate	
Parameter	OR (95% CI)	P value	OR (95% CI)	P value
PVCs burden before ablation	4.23 (2.71–6.99)	<0.01	0.94 (0.78–1.01)	<0.001
Baseline EF	1.21 (0.14–2.18)	<0.05		
Symptom duration	1.09 (0.16–2.09)	<0.05		
SHD	0.62 (0. 42–0.86)	0.7		
Origin of PVCs	0.32 (0.11–0.56)	0.8		
PVCs burden after ablation	1.02 (0.36–2.51)	<0.01	0.92 (0.88–0.99)	<0.001

4.1. RF ablation

Initial success was achieved in 92.2% of the cases, while overall long term success rate excluding recurrent cases was achieved in 80.5% cases. The presence of structural heart disease had no effect neither on initial or long term success rates in the current study with comparable rates of success and recurrence to those reported by other investigators to be influenced by PVC origin, presence or absence of SHD, and the presence of more than 1 focus for PVCs.[21,22] However, mean procedural time, fluoroscopic time, and number of ablation trials were significantly longer in cases with SHD, findings that may give an insight to the technical challenges encountered during ablation in patients with SHD resulting from structural and anatomical alterations encountered in these patients representing significant procedural challenge to operators. Also, LVOT origin was more frequent which is more technically demanding compared to RVOT origin to maintain catheter stability and avoid complications. The overall complication rate in the current study was low with only 1 mortality case due to worsening heart failure.

No significant differences were noted between both study groups regarding baseline or follow-up PVCs burden after successful ablation. Others have reported significantly higher baseline PVCs burden and hence greater percent reduction after successful ablation in patients with SHD,[13,17] which may explain these findings.

4.2. LV function recovery

EF improved significantly nearly in three-fourth of successful cases independent of PVC origin, symptom duration, and the absence or presence of SHD. PVCs burden before and after ablation were the only independent predictors of LVEF recovery after successful ablation. While few recent studies have defined cutoff values for PVCs burden before as previously discussed, a cut off value of <8% for PVCs burden after ablation was defined by our group as an independent predictor of LV function improvement. No definite cut off value was reported in the previous studies but instead the term sustained successful ablation was used which is variable among different investigators while some defined it as complete disappearance others used reduction by >75%, or 80% by the remaining.[9,12,17] Absolute PVCs% reduction may underestimate the hazardous effect of high residual PVCs burden in some patients, though they met criteria of successful ablation. In the current study, patients with significant improvement in EF had mean PVCs burden of 2.4 ± 2.61.

EF improvement occurred as early as 6 months. Relevant data of even earlier recovery were mentioned by many investigators, while others have reported longer periods up to 1 year, though most of the benefit was achieved in the first 6 months. Epicardial foci were associated with more delayed recovery periods up to 45 months.[17,18,23] Obviously, the absence of cases with epicardial foci from the current study may have influenced the early recovery noted. Ischemic patients with previous myocardial infarction had the least magnitude of improvement if any. Relevant data were recently reported.[18] On the other hand, previous reports showed significant improvement in post-myocardial infarction patients.[24] The difference in scar burden may explain this conflict.

In the current study magnitude of EF improvement was comparable between group without previously diagnosed SHD suggested to have “pure PVC-CM” and those with previously diagnosed SHD “mixed PVC-CM” with post-myocardial infarction patients the only exception. In fact, mean EF improvement in patients with SHD after exclusion of ischemic patients was even

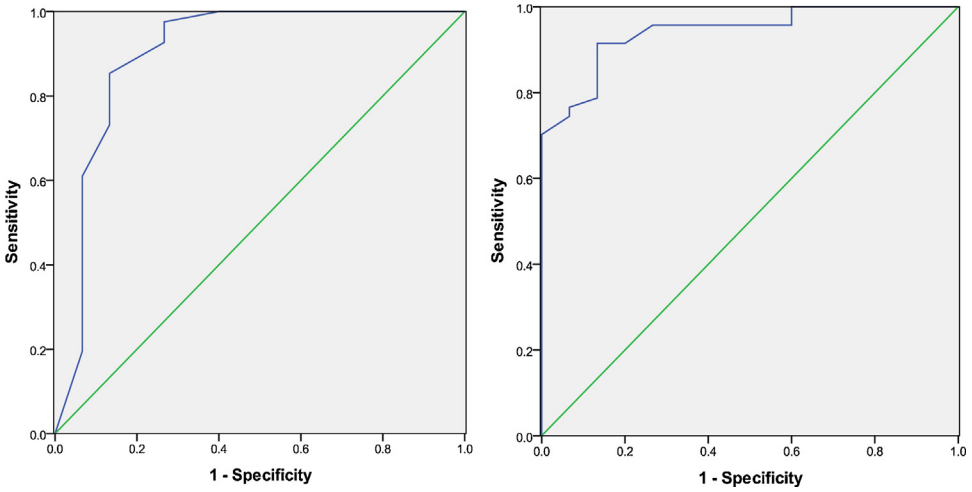

Fig. 3. Receiver of operating characteristics (ROC) curve showing sensitivity and specificity of PVCs burden before (left panel) (AUC = 0.91, $p < 0.001$), and PVCs burden after successful ablation (right panel) (AUC = 0.94, $p < 0.001$) in relation to LVEF recovery.

higher than the idiopathic group. Though conflicting data are reported regarding this specific issue, which can be explained by the heterogeneous study populations, the most consistent is that magnitude of improvement in EF is usually higher in patients with resting LV systolic dysfunction having increased LVEDD and LVESD rather than those with resting normal LVEF, especially in cases where LV dysfunction is purely due to arrhythmic burden rather than those with mixed type which seems quite logic and we totally agree with.[5,16,25]

Nearly 25% of patients with successful ablation did not show significant improvement of LVEF. The short follow-up period, large scar burden in post myocardial infarction patients, residual significant PVCs burden despite meeting criteria of successful ablation, and the absence of direct causal relation between PVCs and LV dysfunction all could explain this. The remaining cases could be regarded as having PVC induced or exaggerated cardiomyopathy, according to the retrospective nature of the diagnosis.

In conclusion, despite that the mechanisms of PVC-CM are not fully understood and the pattern of LV recovery is variable from one patient to the other, all patients with frequent PVCs >10% and impaired LVEF should be considered for RF ablation whether impaired EF is purely "induced" or "exaggerated" by PVCs presence, especially in symptomatic cases. This may prevent further deterioration of LVEF, and decrease or eliminate the need for device implantation.[2,17,26]

4.3. Study limitations

Extended holter monitoring would have given more reliability to the exact PVCs burden before and after ablation given the well known daily variability in PVCs burden. The lack of epicardial ablation facilities forced the exclusion of cases with epicardial PVCs which may have enforced the success rates and excellent early LV recovery. Assessment of exact scar size by cardiac MRI could have given more information in post myocardial infarction patients. The follow up period was relatively short compared with other studies. Lastly, intracardiac echocardiography was not used in the current study and papillary muscle origin was identified initially from ECG, then by activation map and accordingly position of ablation catheter on fluoroscopy, the sensation of the ablation catheter stuck between chordae, and finally intra-procedural bedside echocardiography.

5. Conclusions

PVCs elimination by RF ablation results in significant improvement even restoration of LV function regardless of their origin, duration, or underlying etiology. Post myocardial infarction patients are the least category as regards the magnitude of improvement. PVCs burden before and after ablation are the main determinants for reversal of PVC-CM. The presence of SHD may pose technical challenges during RF ablation but it doesn't affect the clinical response in case of successful ablation.

Conflicts of interest

The authors declare that there are no potential conflicts of interest.

References

1. Sheldon Seth H, Gard Joseph J, Asirvatham Samuel J. Premature ventricular contractions and non-sustained ventricular tachycardia: association with sudden cardiac death, risk stratification, and management strategies. *Indian Pacing Electrophysiol J*. 2010;10(8):357–371.
2. Priori SG, Blomström-Lundqvist C, Mazzanti A, et al. ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J*. 2015;36:2757–2762.
3. Chugh SS, Shen WK, Luria DM, et al. First evidence of premature ventricular complex-induced cardiomyopathy: a potentially reversible cause of heart failure. *J Cardiovasc Electrophysiol*. 2000;11:328–329.
4. Hasdemir C, Ulucan C, Yavuzgil O, et al. Tachycardia-induced cardiomyopathy in patients with idiopathic ventricular arrhythmias: the incidence, clinical and electrophysiologic characteristics, and the predictors. *J Cardiovasc Electrophysiol*. 2011;22:663–668.
5. Fenelon G, Wijins W, Adries E, et al. Tachycardiomyopathy: mechanisms and clinical implications. *Pacing Clin Eletrophysiol*. 1996;19:95–106.
6. Ban JE, Park HC, Nagamoto Y, et al. Electrocardiographic and electrophysiological characteristics of premature ventricular complexes associated with left ventricular dysfunction in patients without structural heart disease. *Europace*. 2013;15:735–741.
7. Betensky G, Robert EP, Francis EM, et al. The V2 transition ratio a new electrocardiographic criterion for distinguishing left from right ventricular outflow tract tachycardia origin. *JACC*. 2011;57(22):2255–2262.
8. Di Base L, Auricchio A, Sorgente A, et al. The magnitude of reverse remodeling irrespective of etiology predicts outcome of heart failure patients treated with cardiac resynchronization therapy. *Eur Heart J*. 2008;29:2497–2505.
9. BeiGe Kang-Ting Ji, Ye Hai-Ge, et al. Electrocardiogram features of premature ventricular contractions/ventricular tachycardia originating from the left ventricular outflow tract and the treatment outcome of radiofrequency catheter ablation. *BMC Cardiovasc Disord*. 2012;12:112.
10. DelCarpio Munoz F, Syed FF, Noheria A, et al. Characteristics of premature ventricular complexes as correlates of reduced left ventricular systolic function: study of the burden, duration, coupling interval, morphology and site of origin of PVCs. *J Cardiovasc Electrophysiol*. 2011;22:791–798.
11. Yokokawa M, Hyungjin MK, Eric G, et al. Relation of symptoms and symptom duration to premature ventricular complex induced cardiomyopathy. *Heart Rhythm*. 2012;9:92–95.
12. Mountantonakis SE, Frankel DS, Gerstenfeld EP, et al. Reversal of outflow tract ventricular premature depolarization induced cardiomyopathy with ablation: effect of residual arrhythmia burden and preexisting cardiomyopathy on outcome. *Heart Rhythm*. 2011;8:1608–1614.
13. Sadron Blaye-Felice M, Hamon D, Sacher F, et al. Premature ventricular contraction-induced cardiomyopathy: related clinical and electrophysiologic parameters. *Heart Rhythm*. 2016;13(January (1)):103–110.
14. Olgun H, Yokokawa M, Baman T, et al. The role of interpolation in PVC-induced cardiomyopathy. *Heart Rhythm*. 2011;8:1046–1049.
15. Simantirakis EN, Koutalas EP, Vardas PE. Arrhythmia-induced cardiomyopathies: the riddle of the chicken and the egg still unanswered. *Europace*. 2012;14:466–473.
16. Baman TS, Lange DC, Ilg KJ, et al. Relationship between burden of premature ventricular complexes and left ventricular function. *Heart Rhythm*. 2010;7:865–869.
17. Panela D, Van Huls Van Taxis C, Aguinaga L, et al. Neurohormonal, structural and functional recovery pattern after premature ventricular complex ablation is independent of structural heart disease status in patients with depressed left ventricular ejection fraction. *J Am Coll Cardiol*. 2013;62:1195–1202.
18. Wojdyła-Hordyńska Agnieszka, Kowalski Oskar, Hordyński Grzegorz J, et al. The effect of radiofrequency catheter ablation of frequent premature ventricular complexes and arrhythmia burden on left ventricular function. *Polish Heart J*. 2017;10.5603/KP.a2017.0058 [on line].
19. Cai CL, Liang X, Shi Y, et al. Cardiac progenitor population that proliferates prior to differentiation and contributes a majority of cells to the heart. *Dev Cell*. 2003;5:877–879.
20. Jongbloed MR, Mahtab EA, Blom NA, et al. Development of the cardiac conduction system and the possible relation to predilection sites of arrhythmogenesis. *Sci World J*. 2008;8:239–269.
21. Yarlagadda RK, Iwai S, Stein KM, et al. Reversal of cardiomyopathy in patients with repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract. *Circulation*. 2005;112:1092–1097.
22. Takemoto M, Yoshimura H, Ohba Y, et al. Radiofrequency catheter ablation of premature ventricular complexes from right ventricular outflow tract improves left ventricular dilation and clinical status in patients without structural heart disease. *J Am Coll Cardiol*. 2005;45:1259–1265.
23. Yokokawa M, Good E, Crawford T, et al. Recovery from left ventricular dysfunction after ablation of frequent premature ventricular complexes. *Heart Rhythm*. 2013;10(2):172–175.
24. Sarrazin JF, Labounty T, Kuhne M, et al. Impact of radiofrequency ablation of frequent post-infarction premature ventricular complexes on left ventricular ejection fraction. *Heart Rhythm*. 2009;6:1543–1549.
25. Jeong YH, Choi KJ, Song JM, et al. Diagnostic approach and treatment strategy in tachycardia-induced cardiomyopathy. *Clin Cardiol*. 2008;31:172–178.
26. Pedersen Christian Torp, Neal Kay G, Kalman Jonathan, et al. EHRA/HRS/APHRS expert consensus on ventricular arrhythmias. *Heart Rhythm*. 2014;11:e166–e196.