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Reversal of left ventricular dysfunction after ablation of premature ventricular contractions related parameters, paradoxes and exceptions to the rule☆

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ABSTRACT

Background: Suppression of frequent premature ventricular contractions (PVCs) does not systematically lead to an expected reversal of PVC-induced cardiomyopathy and determinants of left ventricular ejection fraction (LVEF) recovery (reverse remodeling) after ablation remain largely unknown.
Methods: Ninety-six consecutive patients with a suspicion of PVC induced-cardiomyopathy were retrospectively included. Parameters potentially related to reverse remodeling (>10% increase in LVEF) were analyzed in patients w/wo long-term success (decrease in PVC burden >80%).
Results: Over a mean follow-up of 24 ± 21 months, long-term ablation success was obtained in 76 patients (79%). In these, reverse remodeling was observed in 63 (83%) (LVEF 39 ± 8 to 56 ± 8%, p < 0.0001). In multivariate analysis, only an older age (and marginally a lower PVC QRS amplitude) was independently associated with the lack of reverse remodeling. Only 10 of the 35 patients who initially should have received an ICD for primary prevention remained candidates for implantation after ablation. Lack of reverse remodeling was significantly linked to a higher mortality.
Conclusion: Reverse remodeling was observed in 83% of patients with frequent PVC and unexplained cardiomyopathy undergoing long-term successful ablation of the PVC. A younger age was independently correlated with the occurrence of reverse remodeling.

1. Introduction

Frequent premature ventricular contractions (PVCs) may induce cardiomyopathies, which are characterized by an alteration in left ventricular ejection fraction (LVEF) and left ventricular (LV) dimensions potentially regressive after elimination of the PVCs [1–3].

However, suppression of frequent PVC in patients with unexplained cardiomyopathies does not systematically lead to an improvement in LV function/dimensions (reverse remodeling). Although a few previous studies found that PVC QRS duration, baseline LVEF or the presence of an associated structural heart disease may select those patients without reverse remodeling after elimination of PVCs [4,5], determinants of LV function/dimensions recovery after ablation remain largely unknown.

The aim of this study is to determine the rate of reverse remodeling after ablation in a large multicenter population of patients with cardiomyopathy and frequent PVCs, and to evaluate the factors associated with recovery of LV function/dimensions after PVC ablation.

2. Methods

2.1. Patient population

We retrospectively included all consecutive patients referred for PVC ablation for suspicion of PVC induced-cardiomyopathy (PVCi-CMP) at four European University Hospitals (Toulouse, Bordeaux, Paris Henri Mondor and Lausanne) from 2003 to 2012. PVCi-CMP

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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was suspected in case of decreased LVEF and increased LV dimensions potentially caused by frequent isolated PVCs although a minimal PVC burden was not required. All patients had been optimally treated with cardiac failure medications for at least 3 months and had failed or were intolerant to anti-arrhythmic medications.

2.1.1. Pre-ablation assessment

At baseline, the following data was retrospectively collected:

- PVC morphology (i.e. right or left bundle branch block pattern) and PVC axis on 12 lead ECG
- PVC burden on 24 h ambulatory ECG recordings (averaged when several recordings available)
- Presence of sustained bi/trigeminy (bi/trigeminy burden >5 min on 24 h monitoring)
- LV end-diastolic diameter (LVEDD) and LVEF on transthoracic echocardiography. LVEF was calculated using Simpson method, after at least 3 consecutive sinus beats.

Moreover, during a 30 minute monitoring before ablation, the presence of interpolation (PVC interpolated burden), PVC coupling interval, PVC and sinus beat QRS duration, PVC and sinus beat QRS highest amplitude, and duration of the post PVC pause (when non-interpolated) was determined on an electro-physiological recording system (screen speed 100 or 200 mm/s).

2.1.2. Ablation

Informed consent was obtained for each patient. Anti-arrhythmic drugs were discontinued at least 5 half-lives before the procedure except for amiodarone. Catheters were inserted through venous femoral access and/or through a retrograde arterial or transseptal approach if a LV origin was suspected. The most frequent PVC was then targeted, but sometimes several PVCs were targeted if they seemed to contribute to the LVEF alteration. Isoproterenol perfusion was used when PVCs were absent at the beginning of the procedure. Activation mapping was used together with pace-mapping. Mapping and ablation were performed with non-irrigated or open-irrigated tip catheter, with or without non-fluoroscopic tridimensional systems.

Procedural success was defined by the complete elimination of PVCs at baseline and after repetitive bursts of fast ventricular pacing and isoproterenol infusion.

2.1.3. Follow-up

Patients were seen at outpatient clinics with 24 h ambulatory recording and echocardiography at least once during the first year after ablation, and then regularly especially in case of persisting alterations in LVEF/LV dimensions. Follow-up was assessed after the last ablation in case of repeated procedures. The latest available Holter recording and echocardiography were used for analysis, corresponding to the follow-up duration. Anti-arrhythmic drugs were stopped if success was confirmed the day after the procedure (telemetry monitoring or ambulatory recording) except for patients needing otherwise anti-arrhythmic drugs for supra-ventricular arrhythmias. Beta-blockers and heart failure medications were discontinued only after normalization of LV function and dimensions.

Long-term electrophysiological ablation success was defined by a decrease in PVC burden on ambulatory recording greater than 80% [4,5]. Cardiomyopathy was considered reversible when LVEF increased by more than 10% after RF ablation ("reverse remodeling"). Patients with long-term ablation success were divided in group 1 (presence of reverse remodeling) and group 2 (no reverse remodeling). Patients were considered potentially eligible for ICD in primary prevention (with resynchronization if indicated) if LVEF remained <35% despite PVC ablation [6].

2.1.3.1. Statistical analysis. Continuous variables are expressed as mean ± standard deviation. Categorical variables are presented in percentage and in absolute numbers. Continuous variables are compared using t Student test (or Mann Whitney if non Gaussian distribution). Proportions are compared with χ^2 test. Pairwise comparisons over time are performed using paired *t*-test.

Logistic regression has been performed for determining the parameters associated with the presence of reverse remodeling. All the parameters significantly related to reverse remodeling in univariate analysis ($p < 0.1$) have been considered as eligible explanatory variables in a full multivariate logistic model. Except for age, quantitative variables have been divided into quartiles. Statistics have been performed with the StatView™ software (Abacus Concepts, Inc. Berkeley, CA 1992–1996, version 5.0). A p value <0.05 is reported as statistically significant.

3. Results

3.1. Baseline characteristics of the patient's population

Ninety-six consecutive patients with suspicion of PVC induced-cardiomyopathy were included. Clinical and electro-physiological characteristics of the patients' population are depicted in Table 1.

From these, 29 patients presented with additional structural heart disease (previous myocardial infarction, n = 22, post-hypertensive cardiomyopathy, n = 2, valvular heart disease, n = 3, myocarditis, n = 1, both valvular and ischemic heart disease, n = 1) and were included because most of the alteration in LVEF was suspected to be caused by the frequent PVCs, while 8 additional patients with primary dilated cardiomyopathy were also included because of newly documented frequent PVC and further alteration in LVEF. Six patients were implanted with a resynchronization pace-maker with low biventricular pacing percentage (mean 70 ± 14%) caused by the frequent PVCs. None of the 96 patients had been implanted with an ICD before RF ablation.

Table 1
Clinical and ECG characteristics of the patient's population (n = 96).

Age	53 ± 16
Males	71 (74%)
Anti-arrhythmic drugs	91 (95%)
Beta blockers	80 (83%)
Amiodarone	15 (16%)
Class 1	10 (10%)
Calcium channel blockers	6 (6%)
Sotalol	3 (3%)
Mean number of tested drugs	1.2 ± 0.6
Associated structural heart disease	37 (38%)
LVEF (%)	38 ± 10
LVEDD (mm)	62 ± 8
NYHA class	
I	30%
II	45%
III	17%
IV	8%
PVC burden (%)	26 ± 12
PVC burden <10%	10 (10%)
PVC history	<1 year 15%
	>1 and <2 years 9%
	>2 and <5 years 17%
	>5 and <10 years 19%
	>10 years 8%
	Undetermined 32%
24 h mean heart rate (bpm)	70 ± 9
Bi/trigeminy	78%
PVC coupling interval (ms)	526 ± 94
Post PVC pause (ms)	1113 ± 245
Palpitations	39 (41%)
PVC QRS amplitude (mV)	2.45 ± 0.85
PVC QRS duration (ms)	160 ± 27
Sinus QRS amplitude (mV)	1.78 ± 0.75
Sinus QRS duration (ms)	112 ± 34
Interpolation (%)	14 ± 29
Number of PVC morphologies	1.33 ± 07
Polymorphic PVC	18%
Right bundle branch block PVC pattern	31 (37%)
PVC axis (when monomorphic)	49 right inferior (63%)
	6 right superior (8%)
	16 left inferior (21%)
	7 left superior (9%)

3.1.1. Ablation

A mean of 1.3 ± 0.7 procedure was performed for each patient. PVC originated from the left ventricle (LV) in 66 patients (69%), from the right ventricle (RV) in 21 patients (22%), from the inter-ventricular septum in one, from both ventricles in 7 (8%) and undetermined in one (RV outflow tract n = 20, LVOT/aortic cusp/mitro-aortic continuity n = 27, epicardial - through the CS - n = 23, mitral annulus n = 7, LV/RV apex n = 4, RV inflow tract n = 1, LV/RV septum n = 5 and multiple in 8).

3.1.2. Follow-up

Over a mean follow-up of 24 ± 21 months, long-term ablation success was obtained in 76 patients (79%). Anti-arrhythmic drugs were maintained in 13 patients and BB in 48.

As a result of the ablation procedure, PVC burden decreased significantly from 26 ± 12 to 4 ± 7% ($p < 0.0001$) (Fig. 1) (26 ± 12 to 1 ± 2%, $p < 0.0001$ in the 76 patients with long-term ablation success, and 24 ± 11 to 13 ± 10%, $p < 0.0001$ in the 20 patients considered without long-term success).