REVIEW

Idiopathic Premature Ventricular Contraction (PVC)-Induced Cardiomyopathy: The Role of Catheter Ablation

Sokratis Pastromas, MD

First Department of Cardiology / Electrophysiology and Pacing, Henry Dunant Hospital, Athens, Greece

Abstract

Premature ventricular contractions (PVCs) are common and are considered benign in the absence of structural heart disease. However, high burden of PVCs potentially on 24-hour Holter monitoring, can potentially cause left ventricular dysfunction. In this case, catheter ablation has been demonstrated to be effective at PVC suppression and is associated with improvement or normalization of ventricular function. This form of reversible ventricular dysfunction termed as PVC cardiomyopathy and its pathogenesis is poorly understood at the current time. ***Rhythmos 2019;14(3):51-54.***

Keywords*:* cardiomyopathy, antiarrhythmic therapy, catheter ablation, premature ventricular contractions

Abbreviations: AIC = arrhythmia-induced cardiomyopathy; LV = left ventricular; LVEF = left ventricular ejection fraction; MRI = magnetic resonance imaging; PVC = premature ventricular contraction

Introduction

Premature ventricular contractions (PVCs) are common in daily clinical practice occurring either in patients with structural heart disease or in patients without heart disease. In the latter category of patients, PVCs can cause symptoms of palpitations and when they are frequent could cause reversible left ventricular (LV) dysfunction, characterized as a form of arrhythmia-induced cardiomyopathy (AIC). Idiopathic PVCs are commonly originated from the ventricular outflow tracts, either right or left. Less commonly, other foci such as epicardial tissue, papillary muscles or LV Purkinje system can produce PVCs.[1-4] PVCs could be found in about 40% of 24-hour ambulatory electrocardiogram (ECG) recordings in the general population.[5] Prevalence of PVCs increases with age and is estimated at > 69% in elderly subjects.[5] The association between the presence of PVCs and mortality in patients with recent myocardial infarction was investigated in the Cardiac Arrhythmia Suppression Trial (CAST) I and II. The successful suppression of PVCs with encainide, moricizine and flecainide treatment was associated with increased mortality which was attributed to proarrhythmic effect of those antiarrhythmic agents.[6,7] Later, several studies, reported a significant prevalence of PVCs in their populations. In the ARIC (Atherosclerosis Risk in Communities) study which enrolled over 14000 patients, 6.1% of them had PVCs, and hypertension and obesity were identified as important predictors.[8,9] Moreover, in this population a higher risk of heart failure and sudden cardiac death was reported in patients without known cardiovascular disease and frequent PVCs.[10,11]

PVCs and Left Ventricular Dysfunction

PVC-induced cardiomyopathy is classified as a form of AIC that includes cardiomyopathies induced by atrial or ventricular arrhythmias. The association of frequent PVCs with the development of AIC has been proposed in the literature several years ago. One of the first papers was published from Duffee et al in 1998 who described retrospectively the improvement of LV ejection fraction (LVEF) in a small population of patients with reduced (≤40%) LVEF and frequent PVCs (> 20,000/day) after treatment with amiodarone. [12] It remains unclear how exactly frequent PVCs produce LV dysfunction. [12] One of the proposed mechanisms is that PVC-induced cardiomyopathy is caused by a mechanism similar to tachycardia-induced cardiomyopathy as in other tachy-arrhythmias, such as atrial fibrillation. However, patients with PVCs rarely develop sustained ventricular tachycardia episodes, since the most common form of tachycardia is the repetitive monomorphic ventricular tachycardia. Data from animal studies showed that after ventricular pacing in order to simulate high burden of PVCs, a form of cardiomyopathy was developed which was resolved 2-4 weeks after discontinuation of ventricular pacing without evidence of histopathological changes.[13] According to those data, some authors support the hypothesis that PVC-induced cardiomyopathy could be a result of ventricular dyssynchrony and ventricular remodeling, similar to that caused by left bundle branch block and chronic right ventricular apical pacing.[14,15] Animal studies have not detected cardiac fibrosis as a potential result of frequent PVCs.[16] However, in patients with PVCs and preserved LV dysfunction, echocardiographic evaluation using speckle tracking has revealed slightly reduced left and right ventricular strain indicating a subtle ventricular dysfunction.[17]

Predictors of PVC-Induced Cardiomyopathy and the Role of Catheter Ablation

Epidemiological data have shown that not all patients with PVCs develop AIC. Risk factors have been identified as predictors of LV systolic dysfunction in these patients.

The most important risk factor seems to be the PVC burden which is defined as the percentage of PVCs on the 24h total number of beats. A PVC burden >20% has been associated with the development of heart failure. More specifically, a PVC burden of 24% has been determined as a threshold associated independently with the development of PVC induced cardiomyopathy.[18] Data derived from the population of the Cardiovascular Health Study (subjects with normal LVEF without heart failure symptoms who underwent 24-h Holter monitoring) showed that a PVC burden in the upper quartile (0.123–17.7%) was associated with three-fold greater odds of a decrease in LVEF, a 48% increased risk of heart failure, and a 31% increased risk of death, compared with the lower quartile.[19] Moreover, the risk for the development of heart failure due to PVCs was 8.1% (95% confidence interval: 1.2–14.9%), similar to other heart failure risk factors such as body mass index (BMI), hypertension, age, and coronary artery disease.[19] Moreover, male sex, multiform and asymptomatic PVCs are independent predictors of PVC-induced cardio-myopathy. Epicardial origin as well as wider QRS duration of the PVCs are considered as markers of ventricular dyssynchrony which in turn leads to diastolic dysfunction and mitral regurgitation. The PVC coupling interval has also been studied, without being clear if it plays a role in LV dysfunction.[20,21]

Catheter Ablation in Patients with PVC-Induced Cardiomyopathy

Medical therapy with beta blockers or calcium channels blockers is considered as first line therapy in the management of PVC-induced cardiomyopathy. However, the success rate of PVC suppression varies among different patient categories. Beta blockers have been shown in a randomized trial to decrease PVC burden although they are limited by intolerance and variable effectiveness.[22] Moreover, amiodarone is generally the antiarrhythmic agent of choice in patients with LV dysfunction, however, it is limited by potential toxic effects. The use of Class IC antiarrhythmic agents in patients with cardiomyopathy is not recommended in common clinical practice due to high proarrhythmic risk according to the results of the CAST trial. Nevertheless, a recently published study which enrolled 20 patients with suspected PVC-induced cardiomyopathy who had undergone unsuccessful ablation procedures, reported that treatment with flecainide resulted in a decrease in the mean PVC burden from 36.2% to 10.0%, and an increase in LVEF from 37.4% to 49.0%.[23] Catheter ablation of PVCs in patients with AIC has emerged as an important therapeutic strategy over the last several years especially in the setting of a single PVC morphology and origin from the outflow tract of either right or left ventricle. Comparing ablation to amiodarone, the percentages of successful suppression of PVCs are about 69% and 85% respectively. It should be noted that the discontinuation rate of amiodarone due to adverse effects was 27%.[24] Data from many clinical studies, although the majority of them present retrospective analyses, have shown consistently favorable outcomes on LV function after elimination of PVCs with catheter ablation. Direct comparison of antiarrhythmic drugs versus ablation has been done only in a few clinical trials. Zhong et al. compared the efficacy of ablation and antiarrhythmic drugs in 510 patients with frequent PVCs (40% received drugs and 60% underwent ablation). Catheter ablation reduced significantly the PVCs, especially in patients with more than 10000 PVCs/24h. These patients experienced a greater improvement of LVEF after ablation compared to antiarrhythmic medication.[21] Additionally, in 45 patients who underwent radiofrequency ablation for very frequent monomorphic PVCs, the elimination of the PVCs resulted in significant improvement in LVEF and reduction of end-diastolic and end-systolic diameters of left ventricle after 6-12 months of follow up.[25] Patients who underwent ablation for PVCs due to LV dysfunction, the reduction of the PVC burden to 20% compared to baseline, resulted in recovery of LV systolic function in the majority of them (around 68%) in 4 months.[26]

A similar study was published from Bogun et al who enrolled patients with frequent PVCs and idiopathic dilated cardiomyopathy. Successful ablation of PVCs led to improvement of LVEF. From the study population, 60 patients with PVCs had no response to medical therapy. Twenty-two of these patients with high PVC burden and LVEF <50% underwent ablation, compared with the control group of 11 patients with similar PVC burden and LVEF who did not undergo ablation. LVEF improved from baseline of 34% to 59% ± 7% ($P < 0.0001$) within 6 months in 18 patients who underwent ablation. The control group of 11 patients without ablation had no change in their LVEF over 19 months.[26]

Complications from catheter ablation of PVCs are infrequent and were reported at 2.4% for major complications in a multicenter study. Most common were those which were related to vascular access and pericardial tamponade was reported in 0.8%. [28] Epicardial ablation via sub-xiphoidal puncture should only be performed by qualified operators additionally to endocardial or as first line approach when PVCs meet the criteria of epicardial origin. There are some PVC foci locations for catheter ablation such as LV summit, papillary muscles, and para-

Hisian regions which are associated with lower success rates.

As a successful ablation procedure is considered to be the elimination of PVCs accompanied by normalization or ≥ 10% improvement in LVEF. It is always challenging to predict in which patients with PVC-induced cardiomyopathy the LV function will improve following ablation. Although in these patients, the presence of late gadolinium enhancement on MRI is usually absent, its presence is considered to be a negative predictive factor for LVEF improvement.[29] Other parameters such as the QRS width of the PVC and the duration of QRS during sinus rhythm can be used to assess the possibility of LVEF improvement. [30] Deyell et al. demonstrated that each increase in PVC-QRS duration of 10 ms is associated with an odds ratio of 5.07 (95% CI: 1.2 to 21.01) toward no recovery of the LVEF.[31] This suggests that patients with wider PVC-QRS duration may have more severe underlying cardiac substrate abnormalities.

Conclusion

PVC-induced cardiomyopathy remains poorly understood as regards its pathophysiology and the reasons behind the fact that only some and not all patients show symptoms and signs of heart failure. At this time, catheter ablation is the only therapeutic approach that could improve the LVEF by reducing the burden of or eliminating PVCs. Compared to antiarrhythmic drugs, catheter ablation seems to be more effective without the complications of antiarrhythmic treatment. More data are needed in this field since existing clinical trials are not randomized and only few of them compare prospectively the two therapeutic strategies

References

1. Kim RJ, Iwai S, Markowitz SM, et al. Clinical and electrophysiological spectrum of idiopathic ventricular outflow tract arrhythmias. *J Am Coll Cardiol* 2007;49:2035–2043.
2. Sadek MM, Marchlinski FE. Ablation of ventricular arrhythmias. *Trends Cardiovasc Med* 2014;24:296–304.
3. Yamada T, Doppalapudi H, McElderry HT, et al. Idiopathic ventricular arrhythmias originating from the papillary muscles in the left ventricle: prevalence, electrocardiographic and electrophysiological characteristics, and results of the radiofrequency catheter ablation. *J Cardiovasc Electrophysiol* 2010; 21:62–69.
4. Van Herendael H, Garcia F, Lin D, et al. Idiopathic right ventricular arrhythmias not arising from the outflow tract: prevalence, electrocardiographic characteristics, and outcome of catheter ablation. *Heart Rhythm* 2011;8:511–518.
5. Cha Y, Lee GK, Klarich KW, et al. Premature ventricular contraction induced cardiomyopathy: a treatable condition. *Circ Arrhythm Electrophysiol* 2012;5:229–236.
6. The Cardiac Arrhythmia Suppression Trial II Investigators. Effect of the antiarrhythmic agent moricizine on survival after myocardial infarction. The Cardiac Arrhythmia Suppression Trial II Investigators. *N Engl J Med* 1992;327:227–233.
7. The Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. The Cardiac Arrhythmia Suppression Trial (CAST) Investigators. *N Engl J Med* 1989;321:406–412.
8. Cheriyath P, He F, Peters I, et al. Relation of atrial and/or ventricular premature complexes on a two-minute rhythm strip to the risk of sudden cardiac death (the Atherosclerosis Risk in Communities [ARIC] study). *Am J Cardiol* 2011;107:151–155.
9. Evenson KR, Welch VL, Cascio WE, et al. Validation of a short rhythm strip compared to ambulatory ECG monitoring for ventricular ectopy. *J Clin Epidemiol* 2000;53:491–497.
10. Agarwal SK, Heiss G, Rautaharju PM, et al. Premature ventricular complexes and the risk of incident stroke: the Atherosclerosis Risk In Communities (ARIC) Study. *Stroke* 2010;41:588–593.
11. Agarwal SK, Simpson RJ Jr, Rautaharju P, et al. Relation of ventricular premature complexes to heart failure (from the Atherosclerosis Risk In Communities [ARIC] Study). *Am J Cardiol* 2012;109:105–109.
12. Duffee DF, Shen WK, Smith HC. Suppression of frequent premature ventricular contractions and improvement of left ventricular function in patients with presumed idiopathic dilated cardiomyopathy. *Mayo Clin Proc* 1998;73:430–433.
13. Huizar JF, Kaszala K, Potfay J, et al. Left ventricular systolic dysfunction induced by ventricular ectopy: a novel model for premature ventricular contraction-induced cardiomyopathy. *Circ Arrhythm Electrophysiol* 2011;4:543–549.
14. Lee SJ, McCulloch C, Mangat I, et al. Isolated bundle branch block and left ventricular dysfunction. *J Card Fail* 2003;9:87–92.

15. Tantengco MV, Thomas RL, Karpawich PP. Left ventricular dysfunction after long-term right ventricular apical pacing in the young. *J Am Coll Cardiol* 2001;37:2093–2100.
16. Packer DL, Bardy GH, Worley SJ, et al. Tachycardia-induced cardiomyopathy: a reversible form of left ventricular dysfunction. *Am J Cardiol* 1986;57:563–570.
17. Wijnmaalen AP, Delgado V, Schalij MJ, et al. Beneficial effects of catheter ablation on left ventricular and right ventricular function in patients with frequent premature ventricular contractions and preserved ejection fraction. *Heart* 2010; 96:1275–1280.
18. Baman TS, Ilg KJ, Gupta SK, et al. Mapping and ablation of epicardial idiopathic ventricular arrhythmias from within the coronary venous system. *Circ Arrhythm Electrophysiol* 2010; 3:274–279.
19. Dukes JW, Dewland TA, Vittinghoff E, et al. Ventricular ectopy as a predictor of heart failure and death. *J Am Coll Cardiol* 2015; 66:101–109.
20. Del Carpio 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.
21. Zhong L, Lee YH, Huang XM, et al. Relative efficacy of catheter ablation vs antiarrhythmic drugs in treating premature ventricular contractions: a single center retrospective study. *Heart Rhythm* 2014; 11:187–193.
22. Krittayaphong R, Bhuripanyo K, Punlee K, et al. Effect of atenolol on symptomatic ventricular arrhythmia without structural heart disease: a randomized placebo-controlled study. *Am Heart J* 2002;144:e10.
23. Hyman MC, Mustin D, Supple G, et al. Class IC antiarrhythmic drugs for suspected premature ventricular contraction-induced cardiomyopathy. *Heart Rhythm* 2018;15:159–163.
24. Singh SN, Fletcher RD, Fisher SG, et al. Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia. Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure. *N Engl J Med* 1995;333: 77–82.
25. Takemoto M, Yoshimura H, Ohba Y, et al. Radiofrequency catheter ablation of premature ventricular complexes from left ventricular outflow tract improves left ventricular dilation and clinical status in patients without structural heart disease. *J Am Coll Cardiol* 2005;45:1259 –1265.
26. Yokokawa M, Good E, Crawford T, et al. Recovery from left ventricular dysfunction after ablation of frequent premature ventricular complexes. *Heart Rhythm* 2013;10:172–175.
27. Bogun F, Crawford T, Reich S, et al. Radiofrequency ablation of frequent, idiopathic premature ventricular complexes: comparison with a control group without intervention. *Heart Rhythm* 2007; 4:863–867.
28. Latchamsetty R, Yokokawa M, Morady F, et al. Multicenter outcomes for catheter ablation of idiopathic premature ventricular complexes. *J Am Coll Cardiol EP* 2015;1:116–123.
29. Hasdemir C, Yuksel A, Camli D, et al. Late gadolinium enhancement CMR in patients with tachycardia-induced cardiomyopathy caused by idiopathic ventricular arrhythmias. *Pacing Clin Electrophysiol* 2012;35:465-470.
30. Penela D, Fernandez-Armenta J, Aguinaga L, et al. Clinical recognition of pure premature ventricular complex-induced cardiomyopathy at presentation. *Heart Rhythm* 2017;14:1864–1870.
31. Deyell MW, Park KM, Han Y, et al. Predictors of recovery of left ventricular dysfunction after ablation of frequent ventricular premature depolarizations. *Heart Rhythm* 2012;9:1465–1472.