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Review Article

Current Management of Premature Ventricular Contractions. A Review

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Received: October 15, 2019; **Pubished:** October 22, 2019

Abstract

Premature ventricular contractions are common arrhythmias in patients with or without structural heart disease. Although in the majority of cases they are benign, they can cause symptoms of palpitations, fatigue, dyspnea. Additionally, frequent PVCs can result in cardiomyopathy, that is reversible with treatment of PVCS. In rare cases, PVCs can result in ventricular fibrillation and sudden death. We discuss the etiology and various treatment of PVCs in this article.

Keywords: *Premature Ventricular Contractions; Coupling Interval; PVC Induced Cardiomyopathy; Electrophysiology Study; Radiofrequency Ablation; Sudden Death*

Introduction

Premature Ventricular Contractions (PVCs) are frequently encountered arrhythmias in general population. They are early depolarization of the myocardium originating in the ventricle myocardium, conduction system or purkinje fibers [1]. They are more common in men, in African Americans and in individuals with underlying heart disease (cardiomyopathies, congenital abnormalities, valvular heart disease, ischemia, heart failure), hypertension, hypokalemia or hypomagnesemia. Other common causes of PVCs are anxiety/stress, drugs, and medications (alcohol, amphetamines, caffeine, aminophylline, digoxin), hyperthyroidism, pheochromocytoma, hypoxia and idiopathic [2]. The various mechanisms suggested for premature ventricular contractions include focal activity or reentry from a previous scar or underlying heart disease, triggered activity from after-depolarizations from previous action potential precipitated by drugs such as digoxin or QT-prolonging medications, and enhanced automaticity provoked by catecholamines, electrolyte abnormalities or ischemia. The right or left ventricular outflow tracts are the most common sites of origin of PVCs in the absence of structural heart disease [3].

The majority of PVCs are asymptomatic; some patients report palpitations, dizziness or syncope. The initial evaluation of PVCs should be focused on underlying heart disease. An underlying structural or functional heart disease, even in asymptomatic patients with PVCs is a poor prognostic factor. PVCs with a high burden (> 10%), complex PVCs, polymorphic PVCs, multifocal origin or non-outflow tract origin, abnormal coupling interval, wide QRS, and the increasing frequency with exercise are markers of poor prognosis in patients with PVCs [4]. The diagnostic evaluation, therefore, includes an assessment for underlying structural or functional heart disease or arrhythmia induced cardiomyopathy by electrocardiogram and echocardiography and quantification of the total PVC burden, even in asymptomatic patients with 24-hour ambulatory ECG monitoring.

PVC-induced cardiomyopathy

PVCs were usually considered benign in the absence of underlying heart disease, but recently high PVC burden has been associated with left ventricular dysfunction and dilated cardiomyopathy. The PVC-induced Cardiomyopathy (PVC-induced CMP) was first reported by Duffee., *et al.* in 1998 when they demonstrated improved LV function with suppression of frequent PVCs in patients with presumed idiopathic dilated cardiomyopathy [5]. Yarlagadda., *et al.* demonstrated normalization of LV function with successful ablation of the focal source of ventricular ectopy [6]. Another study demonstrated a progressive worsening of LV function in patients with frequent PVCs [7]. The high PVC burden (> 10%) increases the risk of LV dysfunction and PVC-induced cardiomyopathy. Apart from high PVC burden, the longer duration of the presence of frequent PVCs, PVCs with abnormal coupling interval, an epicardial or right ventricular origin of PVCs, retrograde atrial activation of PVCs, interpolation of PVCs, and a longer PVC QRS duration are also associated with an increased incidence of PVC-induced CMP [1,4,8-10].

The mechanism of PVC-induced CMP is presumed to be related to PVC-induced LV dyssynchrony, abnormal coupling interval, and increased wall stress, leading to LV remodeling and dysfunction. Unexplained left ventricular dysfunction in patients with PVC burdens should raise suspicion for PVC-induced CMP. A therapeutic medical trial or catheter ablation may be considered in patients with LV dysfunction and frequent PVCs if the clinical suspicion for PVC-induced CMP is high. The diagnosis of PVC-induced CMP requires a demonstration of the reversibility of cardiomyopathy with suppression of PVCs. Cardiac magnetic resonance (CMR) is a gold standard imaging modality for the characterization of myocardial tissue and has a role in differentiating PVC-induced CMP from primary cardiomyopathies and in predicting the improvement of left ventricular function [1,8,10].

PVCs and sudden death

PVCs can occasionally result in sudden death due to R on T phenomenon and induction of ventricular fibrillation (VF). Several factors may be involved in the induction of VF- underlying structural heart disease such as Left ventricular hypertrophy, electrolyte abnormalities such ash hypokalemia and hypomagnesemia, Arrhythmogenic right ventricular cardiomyopathy (ARVC) etc. The coupling interval of PVCs to the preceding QRS is frequently fixed causing the PVCs to occur after the end of the previous T wave. Ventricular parasystole occurs when the PVC coupling interval is variable and the inter-ectopic interval is fixed. This occurs due to entrance block into the PVC focus that results in the PVC frequency to be unaffected by the normal QRS. In certain cases, there may be a short R-PVC coupling interval causing risk of VF induction due to R on T phenomenon. We have seen several cases of recurrent VF due to R on T phenomenon that were treated with RF ablation. These PVCs usually occur from within the Purkinje system in our experience- including sites such as Right ventricular moderator band, Right ventricular inflow tract, Right ventricular outflow tract etc. We reported a case of incessant PVCs causing R on T phenomenon and recurrent ventricular fibrillation that required emergency radiofrequency ablation for treatment [11].

Treatment of PVCs

The treatment for patients with PVCs is tailored depending on: (1) whether there is underlying heart disease; (2) the frequency of the PVCs; and (3) the frequency and severity of symptoms. Treatment goals include (1) controlling symptoms; (2) preventing progression to PVC-induced cardiomyopathy if the PVC burden is high, even in patients without symptoms; and (3) improving LV function, if affected. In the absence of heart disease, treatment is based on the PVC burden and presence or absence of symptoms. In asymptomatic patients with low PVC burden (< 10%), no treatment is indicated and the patient should be reassured with no further follow-up [8].

PVC burden is > 10% is associated with LV dysfunction and PVC-induced cardiomyopathy. Therefore, even in the absence of underlying heart disease, the treatment is indicated in patients with high PVC burden and in patients with symptoms. Medical therapy with cardio-selective beta-blockers including atenolol, betaxolol, metoprolol, and nadolol should be considered in these patients to reduce PVC burden and improve prognosis. Alternatively, non-dihydropyridine calcium channel blockers (CCB) can also be used [12]. Amiodarone, a Class III antiarrhythmic agent, can be used if beta-blockers or CCB are unsuccessful in suppressing the symptomatic PVCs. Antiarrhythmic agents

are associated with increased mortality due to their pro-arrhythmic potential [6,8]. No drug is approved by the FDA to treat PVCs. There is no data supporting the use of other antiarrhythmic agents for the suppression of PVCs in asymptomatic patients, especially considering their pro-arrhythmic and other side effects [1]. Ablation may also be useful in patients with frequent and/or symptomatic PVCs refractory to medical therapy. Given the low risk and high success rate of catheter ablation, it should be offered to asymptomatic patients with PVC burden > 10% or symptomatic RVOT PVCs refractory to medical therapy or when medical therapy is not desired, regardless of PVC burden [3].

The presence of underlying heart disease in patients with PVCs is associated with increased mortality. Treatment is focused on correcting the underlying heart disease. In patients with PVCs with left ventricular hypertrophy from hypertension or heart failure, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists and aldosterone antagonists have been shown to decrease mortality [2]. If severe symptomatic PVCs persist despite optimal medications for the treatment of heart failure, amiodarone may be considered. In clinical trials, amiodarone decreased PVCs and did not demonstrate an adverse effect on mortality. Ablation is another option for patients with symptomatic PVCs and heart failure despite medical therapy. In addition to medical therapy, an implantable cardioverter-defibrillator (ICD) may be an option in patients with an ejection fraction of less than or equal to 35 percent with NYHA class II or III heart failure. ICD implantation has been shown to decrease mortality from ventricular arrhythmias compared to amiodarone or placebo [13,14].

Various studies have reported a strong association between increased mortality and high PVC burden in the setting of myocardial ischemia or previous infarction. Suppression of PVCs has not been associated with improved outcomes in various trials. In randomized CAST (Cardiac Arrhythmia Suppression Trial), pharmacological PVC suppression actually worsened survival [15]. In the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT), patients receiving amiodarone for suppression of PVCs post-myocardial infarction had significantly decreased PVCs but no significant change in overall mortality [16]. Therefore, treatment of PVCs in post-infarction patients is symptomatic, unless there is a high burden of PVCs. The treatment, when required, is beta-blockers or class III medications such as sotalol or amiodarone. In Multicenter Automatic Defibrillator Implantation Trial (MADIT), prophylactic therapy with an implanted defibrillator led to improved survival as compared with conventional medical therapy in high-risk patients with coronary heart disease and asymptomatic ventricular tachycardia [17]. Penela D., *et al.* assessed whether ablation might remove primary prevention implantable cardioverter-defibrillator (PP-ICD) indication in patients with frequent PVC. They concluded that in patients with frequent PVC and PP-ICD indication, ablation improves LVEF and in most cases allows removal of the indication [18].

In patients with PVCs with non-ischemic dilated cardiomyopathy including valvular heart disease, lymphocytic and other viral myocarditis, cardiac sarcoidosis, amyloidosis, and other infiltrative diseases, familial conditions, and idiopathic dilated cardiomyopathy treatment is symptomatic, unless the patient has LV dysfunction or a high burden of PVCs. Antiarrhythmic drug therapy, when required, typically involves a beta-blocker or a class III drug such as amiodarone. Ablation can be considered, if medical therapy fails [3,8].

In patients with LV function impairment or PVC-induced CMP, initial treatment is beta-blockers. In patients with mild LV dysfunction, a non-dihydropyridine calcium channel blocker also has good response to arrhythmia. Despite the higher efficacy of the Class I and III anti-arrhythmic drugs, their use is restricted due to potential side effects. Catheter ablation is also an effective treatment option and it should be offered to all patients with high PVC burden and reduced LV function to prevent progression of LV dysfunction and to normalize cardiac function. Amiodarone should only be considered in these patients if they refuse ablation or ablation fails [6,8].

Catheter ablation is a safe and effective treatment for PVCs and can result in an improvement in LV function. It reduces the PVC burden and is curative in most, but it is typically reserved for medically refractory patients. A study by Zhong., *et al.* highlights the superiority of ablation compared to antiarrhythmic drug therapy for treatment of idiopathic PVCs [19]. According to 2019 Consensus on Ablation of Ventricular Arrhythmias, ablation is recommended in the following cases [20]:

- Frequent and symptomatic PVCs originating from RVOT in a normal heart (preferred over medical therapy)
- Treat or prevent LV dysfunction or PVC-induced cardiomyopathy in patients with high burden of PVC
- Recurrent PVCs, from an identifiable site, refractory to antiarrhythmic therapy
- Failure to respond to cardiac resynchronization therapy due to suboptimal pacing due to frequent PVCs
- PVC (fascicular) triggering ventricular fibrillation
- Recurrent symptomatic PVCs in patients with ischemic or non-ischemic heart disease when antiarrhythmic therapy is ineffective or not tolerated or contraindicated

Ablation techniques: RV ablation is individualized after careful evaluation of the patient's ECG and Holter monster. Electroanatomic mapping systems are used to facilitate ablation procedures. Activation mapping is used to identify the earliest signal site of activation using a roving catheter technique. It is ideal for focal PVCs when PVC burden is high. When activation mapping is not possible due to suppression of PVCs or low burden of PVCs, pace mapping is used. In pace mapping, stimulation of PVC site of origin results in QRS morphology of the clinical PVC on ECG. Pace mapping is less specific than activation mapping in localising the PVC site of origin [21]. Figure 1 shows the relationship of RV outflow tract to the Left ventricle and aortic root. Frequently the PVC focus is found in the left coronary cusp or right coronary cusp of the aortic valve. The aortic cusp are posterior to the RVOT.

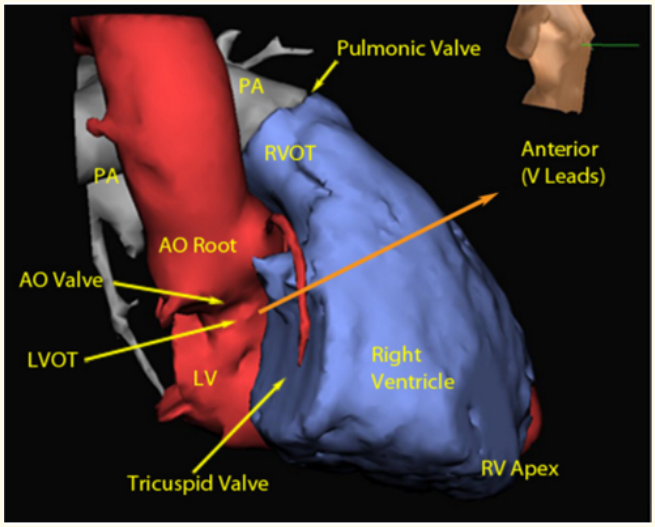

Figure 1

The mapping techniques are combined with fluoroscopy and intracardiac echocardiography for more accurate localization of the ablation site. After ablation, provocative testing with stimulant drugs like isoproterenol is done to confirm non-inducibility of PVCs and to achieve adequate end-points for ablation.

Complications of catheter ablation: The common but generally non-life-threatening complications include femoral vascular events such as hematomas, pseudo-aneurysms, or fistulas that sometimes require subsequent treatment. These complications are generally treatable but can significantly prolong the recovery period. Complications causing permanent disability are also very uncommon but include the risk of collateral injury to the conduction system requiring permanent pacemaker placement, injury to the coronary vessels requiring urgent treatment, or diaphragmatic injury affecting breathing. Left-sided cardiac ablation also carries a small risk of stroke, which is

mitigated by giving intravenous heparin during the procedure. Uncommon but life-threatening complications also include pericardial effusion or cardiac tamponade. A rare complication is a cardiac arrest requiring cardiopulmonary resuscitation [3,22,23].

Case Study 1

55 yr old male with highly symptomatic frequent PVCs and NSVT. Mapping of the RV inflow was performed and a site was found 1.3 cm inferior to HIS bundle recording. Pace mapping showed 95% match on CARTO PASO MODULE (Biosense Webster) or 12/12 match (Figure 2). The yellow dots indicate the location of the HIS Bundle and the red dots are the ablation lesions (Figure 3). Successful ablation performed without damage to the conduction system.

Figure 2 and 3

Case Study 2

70 yr old female with recurrent highly symptomatic PVC in a 50-year-old woman with LBBB. PVC morphology is left bundle and inferior axis. First ablation procedure was unsuccessful. During this the RVOT was mapped. The local bipolar electrogram was 25ms early, the unipolar EGM showed a rS pattern, Pace mapping showed a 95% match on PASO. The electrograms in the LCC/RCC were later. It was determined that the focus was on the LV summit.

During a repeat procedure, Epicardial mapping and ablation performed after pericardial puncture showing the ablation site to be in close proximity to LA. The ablation catheter was positioned near the left anterior descending artery and ablation was performed successfully. The ablation site was approximately 5 mm away from the coronary artery (Figure 4).

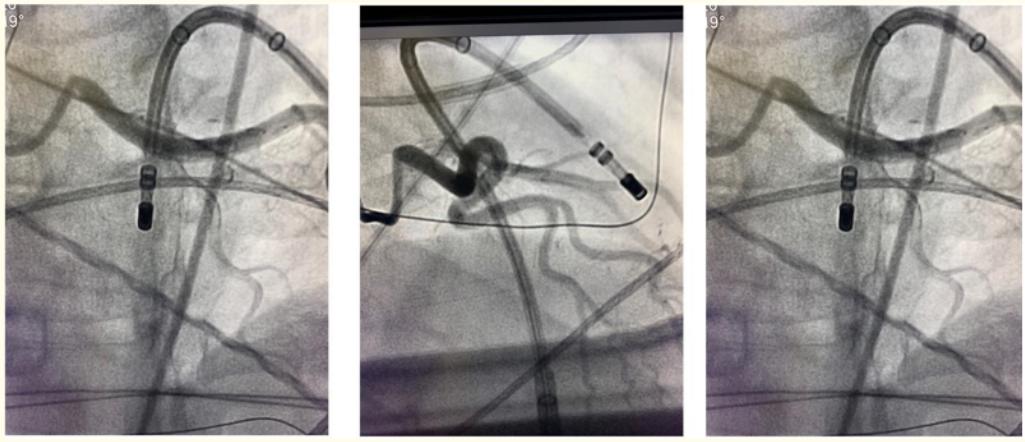

Figure 4

Conclusion

PVCs are commonly seen in the general population. They were thought to be benign in the absence of structural heart disease and were associated with increased mortality in patients with structural heart disease. Recently high burden of PVCs was associated with LV dysfunction and cardiomyopathy. The suppression of PVCs in patients with PVC-induced CMP improves LV systolic dysfunction. The identification of prognostic markers associated with LV dysfunction and reversible cardiomyopathy is important to identify individuals who are at high risk of PVC-induced cardiomyopathy. The treatment depends on the presence or absence of underlying structural heart disease, PVC burden and the frequency and severity of symptoms. The mainstay of medical therapy is cardio-selective beta-blockers. Catheter ablation is a safe and effective treatment for PVCs and can result in an improvement in LVEF.

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Volume 6 Issue 11 November 2019