Editorial

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Insights in Chest Diseases

2016
Vol. 1 No. 3: 22

Premature Ventricular Contraction-Induced Systolic Heart Failure: A Treatable Condition

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Received: June 20, 2016; **Accepted:** June 27, 2016; **Published:** July 07, 2016

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Citation: Casado-Arroyo R. Premature Ventricular Contraction-Induced Systolic Heart Failure: A Treatable Condition. Insights Chest Dis. 2016, 1:3.

Editorial

Ventricular premature depolarizations (VPD) are early depolarizations of the myocardium originating in the ventricle. Traditionally, they have been thought to be relatively benign in the absence of structural heart disease.

VPD-induced cardiomyopathy is a condition in which frequent ventricular ectopic impulses result in left ventricular (LV) dysfunction and heart failure (HF) [1-3]. They are often but not always seen in association with structural heart disease and represent increased risk of sudden cardiac death.

The causal relationship between VPDs and non-ischemic cardiomyopathy (NICM) has been firmly established based on the reversal of the cardiomyopathy with elimination of VPDs using medications or, more commonly in the latter years by using ablation therapy [4]. Identification of the potential risk of VPDs for producing LV dysfunction is essential to provide proper treatment that can improve LV ejection fraction (LVEF) and reduce the incidence of heart failure. The origin of VPDs is diverse. It can be due to abnormal impulse formation, triggered activity or reentry [5, 6]. However, much of the natural history and pathophysiology of VPD-related ventricular dysfunction remains unknown for the moment. In the past, even frequent VPDs were considered to be benign. This affirmation was based on limited clinical studies with a short follow up [7]. It is now recognized that VPDs can exacerbate or even initiate acute HF in patients with preexisting structural heart disease (VPD-induced worsening HF) or can be the sole reason for ventricular dysfunction (VPD-mediated HF).

The animal model (swine, dog) based on chronic rapid pacing has long been recognized to cause depressed LV function and HF [8]. Chronic rapid pacing induces adverse LV remodeling and neurohormonal activation leading to HF. In the same mondel, chronic rapid pacing also has demonstrated to induce several proapoptotic cascades, LV myocyte remodeling and modification in the excitation-contraction process [9-11]. However, as commented before, the mechanism of the relation between VPDs and depression of LV function remains fully unknown. A recent published study suggested that VPD-induced NICM could be primarily functional rather than a fixed abnormality and for that reason in large part reversible with the elimination of the VPD [12]. Other proposed mechanisms related to VPDs are ventricular dyssynchrony and a secondary increase in oxygen consumption. In an animal model, pacing to produce bigeminy could indeed induce a cardiomyopathy without structural changes of the myocardium that was reversible after elimination of the pacing [12]. For all these reasons, it is clear that the scientific community needs a more completely understand the physiologic, molecular and cellular cause of VPD induced/worsened cardiomyopathy.

Several clinical predictors of VPD-induced cardiomyopathy and HF have been identified. Classically, a high VPD burden of more than 24% has been associated with impaired LVEF and HF [13]. A longitudinal study found subclinical deterioration in LVEF over 5 years in those with a high burden of VPDs (≥ 10-20%) [14]. Despite the absence of a definitive and clear cutoff, the risk of developing NICM appears to be greater with a higher VPD burden. A threshold of approximately 10,000 VPDs/day appears required to induce LVEF dysfunction, HF and NICM [13]. Other factors suggested to confer an increased risk of developing NICM include male sex, increased BMI, an epicardial origin, shorter VPD coupling interval (600 ms), interpolated VPDs, the presence of retrograde p waves and asymptomatic nature of VPDs [15-17]. In addition, patients developing VPD NICM were more likely to be paucisymptomatic or to present prolonged palpitations [18]. Other recently published study indicated that patients with VPDs of right ventricular origin presented a higher risk to develop NICM [19]. However, another study has convincingly demonstrated that VPDs from non-outflow tract sites can also induced a NICM

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[13]. In a retrospective analysis, Deyell et al. demonstrated that QRS duration was a predictor of lack of recovery of LV function even after successful ablation of VPDs [20]. The authors also suggested that an increase in VPD duration might be a marker for an increase in fiber disarray due to fibrosis and these patients with subclinical cardiac pathology may be predisposed to developing LVEF dysfunction in the presence of frequent VPDs. In a recently longitudinal published study, Carballeira et al. systematically evaluated the risk factors implicated in the development of VPDs induced HF in patients with more than 10,000 VPDs/day. QRS duration longer than 153 ms and a non-outflow tract site of origin were independently associated with the subsequent development of VPDs induced HF. Interestingly the absolute arrhythmia burden was not associated with the development of LV dysfunction and HF [21].

For the previous reasons, VPD CM is largely under-recognized and the true prevalence is unknown. Some authors have stated that it can represent one third of patients referred for electrophysiological evaluation of VPDs [22]. The diagnosis should be suspected in any patient who presents with frequent VPDs in the presence of an otherwise unexplained LV dysfunction and HF. Since many patients are paucisymptomatic, the presentation can be late and in some cases only after manifest systolic HF develops. In other cases, it can be extremely difficult to determine whether the frequent VPDs are the origin or the consequence of a NICM. Frequently VPDs are considered secondary to the NICM and not treated aggressively. It should be noted that adequate VPD control through medication or ablation is necessary for significant recovery. The management of VPDs in NICM is based on eliminating most if not all of the VPDs, with the goal of improving HF symptoms and reversing LV dysfunction and heart failure. Not only arrhythmia control but also standard medical treatment for heart failure with vasodilators and beta-blockers can mitigate the abnormal neurohormonal response and aid in positive remodeling. In other cases, the correct diagnosis (VPD CM vs. NICM with frequent VPDs) may only be evident after restoration and maintenance of sinus rhythm.

The reversal of the cardiomyopathy with catheter ablation has been firmly established in a recent paper that showed more than 90% of patients achieving long-term VPD control after the ablation [23]. It should be noted that a reduction in VPD burden by 80% has comparable improvement in LV function to complete VPD elimination. The objective is a threshold reduction to less than 5000 VPDs/day required for improvement [4]. Concerning the efficacy of catheter ablation for eliminating VPDs, a recent trial randomized of more than 300 patients with normal LVEF and right ventricular outflow tract VPDs to either medical therapy or ablation. Elimination of VPDs at 1 year was achieved in 80% of the ablation group versus only 12% of the medical group treatment. The ablation group had a 2% incidence of minor complications that all resolved completely before discharge versus 10% in the medical group secondary to the toxicity of the drug therapy [24]. Multiple important observational studies support the findings of the randomized study and point to a potential for an even higher success rate at experienced centers in a near future [17, 19-24].

Elimination of VPDs with ablation has been shown to improve LVEF, ventricular dimensions, functional mitral insufficiency and quality of life in most of the patients [19-25]. It should be noted that elimination of high VPDs burden (>10%) in patients with impaired LVEF could be associated with improvement of LVEF even when structural cardiac abnormalities are present and are not modifiable [4, 20, 25]. Regarding the time to normalization of LVEF after the procedure, in a study of 75 patients with VPD CM who had successful catheter ablation, the mean time to normalization of LVEF was 5 ± 6 months, with almost 70% recovering by 4 months [26]. Several articles have been published recently trying to identify markers for the irreversibility of LV dilated cardiomyopathy in patients with VPDs. Campos et al. described that a unipolar abnormality area cutoff of greater than 32% of total LV surface (10,000/24 h) can be considered as a marker for the irreversibility of LV dysfunction [27, 28].

The workup, treatment, and follow-up of patients with frequent VPDs are summarized in **Figure 1.**

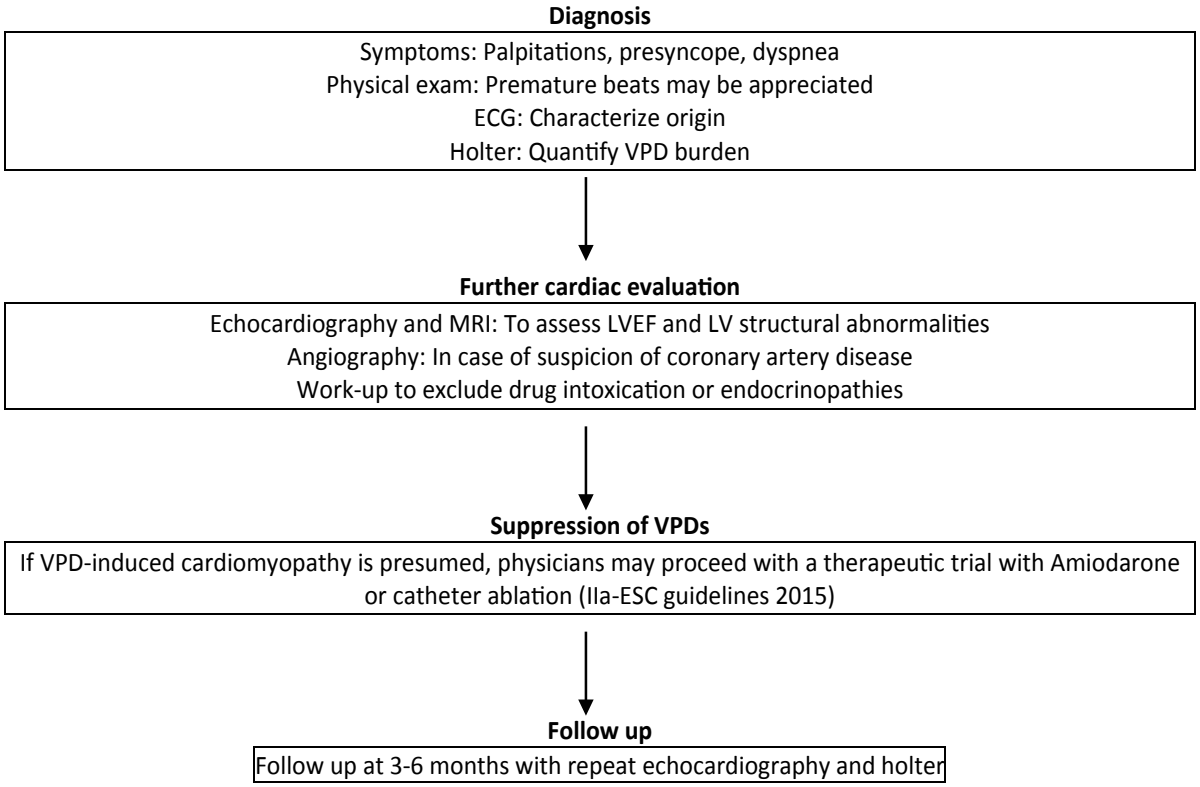

Figure 1 Flow chart for the diagnosis, treatment and follow-up of patients presenting frequent Ventricular Premature Depolarizations (VPDs). ECG: Electrocardiography; LV: Left Ventricular; LVEF: Left Ventricular Ejection Fraction; PVC: Premature Ventricular Contraction.

In conclusion, despite the effort of the scientific community to identify the mechanism of the VPDs induced cardiomyopathy, a lot of questions remain unanswered.

Several associated risk factors have been associated with the evolution to VPDs induce cardiomyopathy. Higher risk patients are those with VPD burden greater than 10,000 and VPD QRS duration greater than 150 ms. Those subgroups warrant close longitudinal follow-up with repeat imaging techniques. Any change in LV chamber size and/or decrease in LV function should be managed aggressively, taking in consideration catheter ablation. NICM caused by frequent VPDs is an important and often under-recognized but potentially reversible cause of cardiomyopathy and HF. Early recognition of the arrhythmia and successful elimination with targeted catheter ablation represents a realistic and unique therapeutic option to reverse a cycle of worsening HF, deteriorating LV function and death [29].

Funding

This study was funded by a postgraduate grant for international research, Spanish Society of Cardiology and Horlait-Dapsens Foundation.

Conflict of Interest

No conflict of interest for this topic.

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