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EDITORIAL

Premature Ventricular Complexes: Benign, Pathogenic or Just a Marker of Myocardial Disease?

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Premature ventricular complexes (PVCs), the commonest electrocardiographic abnormality and cause of palpitations, have long been studied and their significance debated. PVCs in the absence of structural heart disease are generally considered benign, and no treatment is offered for those who are asymptomatic or mildly symptomatic. Beta blockers are often recommended for patients who have symptomatic PVCs or have another indication such as previous myocardial infarction (MI) or left ventricular (LV) dysfunction. There is a paucity of information regarding management of PVCs, particularly in those patients with LV dysfunction, and this is reflected in international guidelines [1,2].

Premature ventricular complexes are common in patients with and without structural heart disease and their incidence and frequency increase with age [3]. Patients may be asymptomatic despite a high burden of PVCs and conversely, highly symptomatic with relatively low frequency of PVCs. Symptoms arise as a result of dyssynchronous ventricular activation and contraction, which likely carries greater haemodynamic significance with increased frequency of PVCs and in patients with pre-existing LV dysfunction. This is the premise for the causal nature of PVCs and the syndrome of ectopic-mediated cardiomyopathy (EMC), which has been highlighted by a number of studies.

An experimental animal study has demonstrated pacemaker simulated PVCs can induce LV dysfunction, and subsequent reversal after withdrawal of the PVC stimulus [4]. In humans, a high burden of PVCs is associated with progressive LV dysfunction when more than 10,000–20,000 beats are detected within 24 hours [5]. A critical threshold for PVC burden >24% for development of EMC has been suggested, and consideration of PVC suppression in the presence of LV dysfunction when PVC burden is >10% [6]. The mechanisms of development of LV dysfunction in this context remain poorly understood.

Anti-arrhythmic drug therapy is associated with adverse effects and a potential for increased mortality in patients with LV dysfunction [7,8]. Compared with anti-arrhythmic drug therapy, catheter ablation has been shown to be more effective in reducing the burden of PVCs [9,10]. Efficacy of catheter ablation of PVCs has been reported to range from 70–100%, and may depend upon PVC origin [11]. Premature ventricular complex origin and its association with LV dysfunction has been variably reported. Threshold PVC burden associated with LV dysfunction has been shown to be lower for right compared to left ventricular PVCs, as well as for epicardial or non-outflow tract PVCs [12–14].

While PVCs are known to reduce the effectiveness of cardiac resynchronisation therapy (CRT) and are associated with worsening heart failure and increased mortality in this population, randomised studies of PVC elimination in the context of LV dysfunction are lacking [15,16]. Elimination of

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high burden PVCs (>10,000 beats in 24 hours) in CRT non-responders has demonstrable improvement in LV function, LV indices and New York Heart Association functional class [17]. Further, EMC has been demonstrated to be a potentially reversible condition by elimination of PVCs by catheter ablation [18]. A meta-analysis of catheter ablation for frequent PVCs included a subgroup analysis of patients with LV dysfunction totalling 336 participants; and elimination of PVCs resulted in a mean increase from baseline left ventricular ejection fraction (LVEF) of 35.1% by 12.4% [19].

In this issue, Lee et al. sought to clarify the predisposing risk factors for EMC and describe the outcomes for patients presenting for PVC or idiopathic ventricular arrhythmia (VA) catheter ablation with (n = 54 [36%]) or without (n = 98 [64%]) LV dysfunction [20]. Left ventricular dysfunction was defined as a left ventticular ejection fraction (LVEF) <50%, and median LVEF was reported to be 40% (32–45%). The majority of previously published studies included patients with more severe LV impairment who may have derived greater benefit from PVC elimination [19]. In the current cohort [20], patients with LV dysfunction were older (mean 59 +/− 15 years) and more likely to be male n = 40 (74%) compared to those with normal systolic function. Consistent with previous studies, patients with LV dysfunction more often have PVCs originating from the right ventricular outflow tract. Patients with LV dysfunction were more symptomatic of heart failure by NYHA functional class, and conversely had less symptoms of palpitations, chest discomfort and dizziness. Patients with cardiomyopathy, as expected, were more likely to be treated with heart failure therapies and despite this, had ongoing LV systolic dysfunction. Premature ventricular complex burden appeared to be inadequately controlled despite use of amiodarone in 22% of patients with LV dysfunction. Post-ablation PVC burden was significantly reduced from 29% to 1%. Improvements in LVEF were demonstrable in 59% of patients with paired transthoracic echocardiograms pre- and post-procedure, with median LVEF increasing from 40% to 52%.

The prognostic implications for patients with PVCs remains controversial. The causative nature of PVCs remains difficult to prove given PVCs may also be the result of an underlying cardiomyopathy. The mere presence of PVCs may be a marker of myocardial disease or cardiovascular risk. Early studies demonstrating an association with increased mortality, have been criticised due to an inability to exclude underlying cardiac disease based on their methodology [21,22]. However, one recent observational study showed that even relatively low PVC burden (>12 beats per day) was associated with a higher incidence of all-cause mortality, cardiovascular hospitalisation, all-cause hospitalisation and new onset heart failure independent of other clinical risk factors [23]. Conversely, in patients with LV dysfunction, PVC frequency has been shown not to have any bearing on survival [24].

While PVCs are a frequent occurrence both in patients with structurally normal hearts and in those with LV dysfunction, the associated factors that determine an adverse prognosis remain elusive. In light of available research, the landscape has not changed in the assessment of, and indeed treatment of patients with PVCs and LV dysfunction. Patients presenting with PVCs need careful assessment for underlying structural heart disease, and ongoing surveillance and treatment in the absence of LV dysfunction should be considered. Catheter ablation with a goal of PVC elimination appears to be useful in patients with LV dysfunction who are not responding to medical therapies and CRT. Lee et al. have demonstrated that, after multivariate analysis, only male gender was predictive of cardiomyopathy in their cohort [20]. This study reinforces the notion that EMC is a potentially reversible syndrome and PVC treatment with catheter ablation in the context of LV dysfunction should be strongly considered. Further research is needed to guide management of patients with PVCs and LV dysfunction, clarify the risk factors and pathogenesis of EMC, and its treatment.

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