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EDITORIAL COMMENT

Retrograde Transvenous Ethanol Ablation of Refractory Premature Ventricular Contractions

Re-Evaluating the Electrophysiologist's Toolbox*

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Frequent premature ventricular contractions (PVCs) have been demonstrated clinically and in animal models to cause cardiomyopathy (1,2), although the precise mechanism remains an area of active investigation (3). Catheter ablation is a Class I recommendation (Level of Evidence: B-NR) for the treatment of patients with cardiomyopathy attributable to frequent, monomorphic PVCs in whom antiarrhythmic drugs are ineffective or otherwise unsuitable (4,5). However, in patients in whom a traditional endocardial approach is unsuccessful, alternative/adjunctive methods may be considered (6).

In this issue of *JACC: Case Reports*, Meier et al. (7) describe the case of a young man referred for ablation of incessant PVCs with an associated reduced left ventricular ejection fraction (LVEF) of 40%. He had been found to have a 30% PVC burden 7 years earlier, at which time his LVEF was normal. Due to the refractory nature of his PVCs, following a trial of beta-adrenergic blockade and amiodarone antiarrhythmic drug therapy, he had undergone an unsuccessful attempt at PVC ablation via retrograde aortic approach 6 years prior to presenting to the authors. His electrocardiogram (ECG) demonstrated a right bundle branch block pattern in V_1, with a rightward and inferior axis and V_4 transition, suggestive of a basal-mid lateral left ventricular (LV) focus.

In addition, the ECG had features suggestive of an epicardial origin, including a QS pattern in lead I, absence of inferior Q waves, and a pseudo-delta wave in lead V_1 (8). Combining these findings with the unsuccessful initial ablation, the authors chose an endocardial approach for the redo ablation with transseptal LV access, rather than a retrograde aortic approach. Ultimately, however, they pursued their backup option of retrograde transvenous ethanol ablation (TVEA) via the coronary venous system due to an inability to suppress the PVCs with prolonged lesions from the LV endocardial surface. In total, the authors administered 2 ml of 96% ethanol via an ablation catheter positioned in an anterolateral vein after confirming transient suppression of the PVCs with cold saline infusion at the same location. Despite acute procedural success, the patient unfortunately had recurrence of PVCs, at a reduced frequency, 4 weeks post-ablation and was subsequently lost to follow-up.

We commend the authors for their efforts to treat a challenging case of premature ventricular contraction-induced cardiomyopathy (PVCi-CMP), in which an endocardial ablation was unable to successfully suppress the arrhythmia. In a study of 168 patients referred for PVC ablation, epicardial origin, high PVC burden, and lack of palpitations were associated with development of PVCi-CMP (9), at least 2 of which were observed in the patient presented by Meier et al. (7). In another series of 264 patients with frequent idiopathic PVCs and LV

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dysfunction, among those in whom the PVC burden was reduced to <20% of the initial burden, 68% had recovery of LV function within 4 months (10). In those who did not experience recovery in the first 4 months post-ablation, 54% had an epicardial origin of PVCs, and epicardial PVC origin was the only predictor of delayed LV recovery in multivariate analysis, underscoring the importance of aggressive treatment in young, otherwise healthy patients.

Although the authors acknowledged the lack of definitive proof of an epicardial origin via mapping within the pericardial space or coronary veins, the preponderance of evidence, including the ECG, intraprocedural findings, and the area of retained viability seen on cardiac magnetic resonance imaging post-ablation, suggested this was the case. Intracardiac echocardiography would have helped delineate intracavitary structures, such as the anterolateral papillary muscle, and allow a better understanding of the anatomic correlation with the arrhythmia source. Further mapping of the coronary venous system could have been performed prior to TVEA using unipolar intracoronary wire mapping, as described for intramural ventricular septal substrates (11). This may have been helpful to limit endocardial ablation lesions leading to edema and alterations of the substrate, which may have limited the success of subsequent TVEA. An alternative option to enhance lesion depth from the endocardial surface involves use of a higher-impedance irrigant, such as half-normal saline, which has shown promise in a multicenter study (83% acute success in refractory PVC/VT ablation), although with a higher risk of steam pop (12.6%) (12).

Alternatively, given the absence of a previous sternotomy or other known contraindication, a more invasive, yet safe, approach involving pericardial access could have been pursued for potentially enhanced diagnostic and therapeutic yield (13). Pericardial access requires careful planning for optimal outcomes, including minimization of risk to the patient. As shown in 1 series of 309 ablation procedures in 277 patients, epicardial access was successfully obtained in 94%, but ablation in the pericardial space was not possible in 28% of cases and limited in 7%, due most often to failure to identify a target (15%) and proximity to a coronary artery (13%) (14). Another large series of 163 patients had similar findings in which approximately one-third of patients who had epicardial access obtained did not undergo epicardial ablation (15), highlighting the need for improved substrate localization to guide these procedures. Epicardial access would facilitate other approaches with potential advantages in treating intramural or epicardial arrhythmias, including simultaneous unipolar ablation and bipolar ablation techniques, which have been shown to improve lesion size and transmurality (16).

Use of ethanol for successful transcoronary chemical ablation of ventricular tachycardia (VT) in 3 patients with ischemic heart disease was described by Brugada et al. (17) following earlier work in dogs by Inoue et al. (18). In a contemporary series of transcoronary arterial ethanol ablation (TCEA), Sacher et al. (19) reported on 9 patients (7 men, age 55 ± 9 years) treated for symptomatic VT after at least 1 failed radiofrequency ablation attempt. Acute procedural success, defined by noninducibility of VT, was achieved in 8 of 9 (89%) for the clinical VT, and 56% for any inducible VT at the termination of the procedure. During a mean follow-up of 29 ± 23 months, 5 patients were either free of VT or had significant burden reduction, but 3 others died of refractory heart failure, and 1 underwent cardiac transplantation. A follow-up study from the same group reported similar findings in another 22 patients offered TCEA, with 82% acute success, 64% VT recurrence in follow-up, and 32% overall mortality (20).

TVEA, as employed in the case by Meier et al. (7), has even more limited data surrounding its use and outcomes. Kreidieh et al. (21) reported a series of 7 patients undergoing PVC/VT ablation (previous failed ablation in 6), in whom TVEA was attempted by delivering 98% ethanol into a septal branch of the anterior interventricular vein (n = 5), a septal branch of the middle cardiac vein, and a posterolateral coronary vein. Despite acute success in all patients, over 590 ± 722 days average follow-up, VT recurred in 4 of 7 (57%), 3 of whom underwent successful redo radiofrequency ablation. The cumulative TCEA and TVEA data highlight the promise of this therapy for refractory PVC/VT patients, especially those with no alternative options, but there are still many unknowns regarding ethanol ablation for a young patient with PVCi-CMP. The appropriate dose of ethanol and number of injections remain to be determined. Early TCEA studies used 1.5 to 6 ml of 96% ethanol per patient (18), whereas Sacher et al. (19) used 1 to 5 ml (in 1-ml increments), and Kreidieh et al. (21) reported 1-ml injections up to a total of 4 ml, noting that all cases of VT recurrence occurred in those who received only 1 ml of 98% ethanol. Other potential limitations with TVEA include dependence on vessel anatomy, ethanol spillover and collateral damage to surrounding structures (potentially greater than an arterial approach), and complications of catheterization and balloon inflation (16,21,22).

The case presented by Meier et al. (7) highlights the potential as well as some of the challenges inherent to TVEA for treatment of refractory PVCi-CMP. Although much of the available published data for TCEA and TVEA includes a population of patients who are older and have a higher burden of comorbidities, additional studies will be helpful to elucidate the role of ethanol ablation in patients with frequent PVCs. Careful consideration of alternative options for challenging epicardial substrates, such as utilization of half-normal saline, simultaneous unipolar or bipolar ablation, and ethanol ablation, should be undertaken to optimize the risk-benefit ratio for each individual patient.

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