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EDITORIAL COMMENT

Ventricular Arrhythmia in the Left Ventricular Assist Device Patient

When You Can't Ablate, Denervate*

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Cardiac sympathetic denervation (CSD) has demonstrated clinical benefit in patients with advanced heart failure (HF) who are experiencing ventricular arrhythmias (VAs). CSD is included in the 2017 joint guidelines of the American Heart Association, the American College of Cardiology, and the Heart Rhythm Society as a reasonable therapy in patients with ventricular tachycardia (VT) or ventricular fibrillation storm who are not suitable candidates for catheter ablation because it would be ineffective or not an option (1,2). Patients with advanced HF who require left ventricular assist device (LVAD) support are at risk for concomitant VAs. In addition to the underlying cardiomyopathy, LVAD implantation can further increase the risk for VAs through mechanical factors such as right ventricular dysfunction and suction events. However, limited data exist for CSD after LVAD implantation.

In this issue of *JACC: Case Reports*, Vlismas et al. (3) present the case of a 46-year-old woman with a history of nonischemic cardiomyopathy with an implantable cardioverter-defibrillator (ICD) who developed late VAs 1.5 years post-LVAD implantation. Antiarrhythmic therapy had failed, and the patient was deemed a suboptimal candidate for an epicardial approach to VT ablation. Although listed for cardiac transplantation, she was highly sensitized, as determined by panel-reactive antibody testing, and therefore underwent bilateral CSD (BCSD) successfully and without complications.

The significance of late VAs post-LVAD remains controversial. The multicenter ASSIST-ICD (Determination of Risk Factors of Ventricular Arrhythmias After Implantation of Continuous Flow Left Ventricular Assist Device) study identified late VAs after LVAD implantation in 26.9% of patients, but this finding was not associated with worse survival (4). In contrast, patients with LVADs who experienced electrical storm, defined as at least 3 episodes of sustained VAs with a 24-h period, did have a decrease in 1-year survival (5). Management of post-LVAD VAs typically includes antiarrhythmic therapy and catheter ablation. Several small cohorts that span the evolution of LVAD technologies have demonstrated benefit of catheter ablation for post-LVAD VA. A more recent, larger, single-center study of 21 patients with continuous-flow LVADs for destination therapy demonstrated improved 1-year survival with reductions in recurrent VA, recurrent ICD therapies, and amiodarone use (6). In the presented patient with recurrent ICD therapies, although she was not a considered a good candidate for catheter ablation, treatment of her VA was warranted to potentially improve her quality of life.

Whether post-LVAD VAs are macro-re-entrant, micro-re-entrant or focal, the autonomic nervous system is critical to the initiation and maintenance of VAs. Interestingly, basic and translational studies have consistently shown that LVAD implantation improves autonomic tone, with a potential beneficial

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effect on the risk of VAs. Although tilt-table testing in patients with HF and continuous-flow LVADs demonstrated increased sympathetic nerve activity (7), the preponderance of evidence suggests reduced sympathetic tone post-LVAD implantation. Despite the hypothesis that the minimal pulsatile flow may reduce baroreceptor reflex sensitivity, the low pulse pressure of continuous-flow LVADs suffices to maintain baroreflex-mediated restraint on the sympathetic nervous system (8). Additionally, biochemical and molecular markers suggest improvement in the neurohormonal axis in these patients. For instance, measurement of plasma levels of neurohormones was decreased at the time of LVAD explantation or cardiac transplantation (9). Mechanical unloading from LVAD implantation in failing human hearts improved ß-adrenergic receptor expression and responsiveness at the time of transplantation (10). In a study of 12 patients with LVADs, along with recovery in hemodynamic, echocardiographic, and biochemical parameters, improvement in sympathetic innervation on iodine-123 metaiodobenzylguanidine imaging was noted (11). Higher rotational speeds may reduce sympathetic activity further, in addition to improvements in left ventricular remodeling in patients with a higher ratio of sympathetic to parasympathetic tone (12). Therefore, although the autonomic nervous system is a key player in the pathogenesis of VAs, LVAD implantation itself may improve sympathovagal balance.

Despite evidence for improved autonomic tone post-LVAD implantation, CSD may provide further autonomic modulation in patients with LVADs who experience VAs. However, data are limited. Ablation is an appropriate initial intervention for many patients with LVADs, but there are cases where ablation is suboptimal or where experienced operators are not available to undertake a complex ablation. Further, as in the presented case, patients with polymorphic VT or ventricular fibrillation may not have clear anatomic substrates to target. In such instances, other options should be considered. A previous case report demonstrated the benefit of CSD in a patient with an LVAD who developed VAs (13). A 72-year-old man with HF who had undergone LVAD and ICD implantation developed recurrent VT refractory to catheter ablation and underwent left-sided CSD. That patient did experience recurrence of VA at 55 days post-sympathectomy. BCSD appears to be superior to left-sided CSD to limit VA recurrence, and the addition of right-sided CSD may further improve freedom from VA recurrence (1). The patient in the presented case underwent BCSD, and it will be interesting to see how the patient fares in the long term. Because BCSD may also delay the need for cardiac transplantation compared with left-sided CSD alone, the procedure may provide enough time for desensitization therapy before cardiac transplantation (1). Furthermore, as Vlismas et al. (3) mention, successful treatment with CSD may allow for discontinuation of amiodarone to reduce risk of primary graft failure.

In conclusion, patients with post-LVAD VAs who undergo unsuccessful ablation or who are not good candidates for ablation should be considered for CSD. Although LVAD implantation seems to improve sympathovagal balance, the current case suggests that some patients may benefit from additional autonomic modulation after CSD. However, further clinical and translational understanding is required for appropriate patient selection.

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