Cardiac sympathetic denervation in patients with refractory ventricular arrhythmias or electrical storm: Intermediate and long-term follow-up

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BACKGROUND Left and bilateral cardiac sympathetic denervation (CSD) have been shown to reduce burden of ventricular arrhythmias acutely in a small number of patients with ventricular tachyarrhythmia (VT) storm. The effects of this procedure beyond the acute setting are unknown.

OBJECTIVE The purpose of this study was to evaluate the intermediate and long-term effects of left and bilateral CSD in patients with cardiomyopathy and refractory VT or VT storm.

METHODS Retrospective analysis of medical records for patients who underwent either left or bilateral CSD for VT storm or refractory VT between April 2009 and December 2012 was performed.

RESULTS Forty-one patients underwent CSD (14 left CSD, 27 bilateral CSD). There was a significant reduction in the burden of implantable cardioverter-defibrillator (ICD) shocks during follow-up compared to the 12 months before the procedure. The number of ICD shocks was reduced from a mean of 19.6 ± 19 preprocedure to 2.3 ± 2.9 postprocedure ($P < .001$), with 90% of patients experiencing a reduction in ICD shocks. At mean follow-up of 367 ± 251 days postprocedure, survival free of ICD shock was 30% in the left CSD group and 48% in the bilateral CSD group. Shock-free survival was greater in the bilateral group than in the left CSD group ($P = .04$).

CONCLUSION In patients with VT storm, bilateral CSD is more beneficial than left CSD. The beneficial effects of bilateral CSD extend beyond the acute postsympathectomy period, with continued freedom from ICD shocks in 48% of patients and a significant reduction in ICD shocks in 90% of patients.

KEYWORDS Sympathectomy; Cardiac denervation; Ventricular arrhythmias; Electrical storm

ABBREVIATIONS **CSD** = cardiac sympathetic denervation; **EF** = ejection fraction; **ICD** = implantable cardioverter-defibrillator; **PAP** = pulmonary artery pressure; **VT** = ventricular tachyarrhythmia

(Heart Rhythm 2014;11:360–366)

Introduction

The autonomic nervous system is known to play a role in the genesis and maintenance of ventricular arrhythmias.[1,2] Currently, antiarrhythmic therapies and catheter ablation represent the standard of care in patients with recurrent ventricular tachyarrhythmia (VT) and implantable cardioverter-defibrillator (ICD) shocks. Neuromodulation is increasingly emerging as an alternative therapy, with benefits of thoracic epidural anesthesia, cardiac sympathetic denervation (CSD), and spinal cord stimulation shown in animal models and case series of patients with and without cardiomyopathy.[3–9] Left CSD has also shown benefit in the setting of refractory VT and long QT syndrome or catecholaminergic polymorphic VT.[10–12] Left and bilateral sympathectomies, involving removal of the lower third to lower half of the stellate ganglion and T2–T4 sympathetic ganglia, have shown short-term benefit in the setting of VT storm and VT refractory to medical therapy in a small number of patients with cardiomyopathy. The benefits of left and bilateral CSD beyond the acute postprocedure period are unknown. The purpose of this study was to assess the intermediate and long-term effects of CSD in patients with cardiomyopathy and refractory VT.

This study was supported by NHLBI R01HL084261 to Dr. Shivkumar and AHA National Award #11FTF755004 to Dr Vaseghi. **Address reprint requests and correspondence:** Dr. Marmar Vaseghi, UCLA Cardiac Arrhythmia Center, 100 Medical Plaza, Suite 660, Los Angeles, CA 90095. E-mail address: mvaseghi@mednet.ucla.edu.

Methods

Retrospective review of data was approved by the University of California, Los Angeles Institutional Review Board.

1547-5271/$-see front matter http://dx.doi.org/10.1016/j.hrthm.2013.11.028

Patient population

Data from 41 patients with VT storm or refractory ventricular arrhythmias and ICD shocks who underwent CSD between April 2009 and December 2012 were reviewed. The type, cause, treatment of ventricular arrhythmias, type of CSD (left or bilateral), and procedural data and complications were reviewed in all patients. VT storm was defined as three or more episodes of sustained VT within a 24-hour period, each of which required termination by an intervention. Refractory VT was defined as recurrent ICD shocks that did not response to antiarrhythmic, medical, or catheter ablation therapy.

Cardiac denervation procedure

All patients underwent either left or bilateral CSD. The first five patients in this series, between 2009 and 2010, only underwent left CSD, given the greater number of animal and human studies in support of left CSD compared to bilateral CSD at the time.[7,8] The decision to perform left or bilateral CSD also was partly driven by the patient's ability to tolerate the longer general anesthesia/procedure time required for bilateral CSD. Left CSD was often performed at the same time as right CSD. However, left CSD was always performed first. CSD was performed using video-assisted thoracic surgery in all patients. CSD consisted of resection and removal of the lower third to half of the stellate ganglia and T2–T4 thoracic ganglia as well as transection of the nerve of Kuntz, when present. The lower third to half of the stellate ganglia was removed to avoid Horner syndrome, as the ocular neural fibers generally cross at the upper half of the stellate ganglia. With the patient under general anesthesia, the ipsilateral lung was deflated and not ventilated, using a double-lumen endotracheal tube. Three 1.5-cm incisions were made in the ipsilateral subaxillary area. The left thoracic sympathetic chain was identified behind the parietal pleura, and the lower half of the stellate ganglion together with the thoracic ganglia at the T2–T4 level were dissected and removed. Histologic confirmation of neuronal cell bodies within the ganglia was obtained intraoperatively. The nerve of Kuntz (an intrathoracic nerve that connects the first and second thoracic nerves, bypassing the sympathetic chain between the T2 ganglion and stellate ganglion in some patients) was sought and divided in order to complete the sympathectomy.[13] Chest drains were placed and removed within 24 hours after confirmation of lung reexpansion and lack of a pleural effusion.

Follow-up

Hospitalization records, outpatient visits, and ICD interrogations were used to determine the outcome of CSD during follow-up. If the patient, next of kin, or referring physicians could not be contacted, the National Death Index was used to determine if the patient was deceased. Echocardiograms were used to assess follow-up left ventricular ejection fraction (EF) and pulmonary artery pressures (PAPs). For follow-up of ICD shock status, inpatient and outpatient notes and ICD interrogations were obtained and reviewed. In addition, phone calls to the primary physician, patient, or immediate relatives of deceased patients were made. Burden of ICD shocks was assessed from ICD interrogations and physician notes, and the data were included only if ICD interrogations or physician documentation of number of shocks before the procedure and during follow-up could be obtained.

Statistical analysis

Continuous variables are summarized as mean ± SD or median when appropriate. Comparison of outcomes between left and bilateral CSD was made using the Fisher exact test, and comparison of ICD burden, EF, and PAP pre- and postprocedure was made using the Wilcoxon signed rank test. All statistical analysis was performed using SAS software (version 9.1, SAS institute Inc, Cary, NC). $P < .05$ was considered significant. Cumulative shock-free survival and cardiovascular mortality were calculated using Kaplan-Meier curves and tested in subgroups by the log-rank test for trend. For these analyses, time to first shock or death post-CSD was calculated, and data are displayed as cumulative event-free survival. For Kaplan-Meier analysis of freedom from ICD shock only, the patients who were lost to long-term follow-up were censored at time of last follow-up.

Results

Patient characteristics

Forty-one patients (35 male; age 59 ± 13 years) who presented with either VT storm or recurrent ICD shocks refractory to medical therapy and catheter ablation underwent CSD. Fourteen patients (12 male; age 63 ± 11.3 years) underwent left CSD only and 27 patients (23 male; age 57 ± 14 years) underwent bilateral CSD (Table 1). Patients were taking a median of 2 (range 1–3) antiarrhythmic medications, usually amiodarone and lidocaine or mexiletine, and 73% were taking beta-blockers before the procedure. In the remaining 27% of patients, beta-blockers were not tolerated because of low blood pressure at presentation. Thirty-eight patients had undergone previous catheter ablation procedures. The median number of VT ablations before CSD was 2 (range 1–5). The three patients who had not undergone a VT ablation procedure had presented with polymorphic VT or idiopathic ventricular fibrillation and were deemed inappropriate candidates for catheter ablation.

Left CSD

Of the 14 patients who underwent left CSD, 7 (50%) had nonischemic cardiomyopathy, 5 (36%) had ischemic cardiomyopathy, and 2 patients had hypertrophic cardiomyopathy (Table 1).

Bilateral CSD

Of the 27 bilateral CSD patients, 15 (56%) had nonischemic cardiomyopathy, 4 (15%) had ischemic cardiomyopathy, and 2 had cardiac sarcoidosis. In addition, one hypertrophic, one chagasic, one arrhythmogenic right ventricular dysplasia,